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RING ULCER OF THE CORNEA

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CHICAGO

A review of the literature reveals a certain confusion with regard to conditions which may be called ring ulcer of the cornea. Fuchs [1] in 1893 described what he called metastatic marginal ulcer. It occurred in old people with multiple fine punctate infiltrations in the superficial parenchyma near the limbus. "For a time," he stated, "they resemble marginal superficial punctate keratitis, but frequently break down to form marginal ulcers crescentic with the limbus. They tend to heal rapidly but recur." He also described the occasional confluence of several catarrhal ulcers to form an annular ulcer completely encircling the cornea and stated that deep penetration of such an ulcer may cause ectasia of the cornea. De Schweinitz [2] described a severe form of ring ulcer, seen in debilitated persons, in which the central part of the cornea is girdled and cut off from its nutrition, with perforation of the cornea and prolapse of the iris in some cases. He also described milder forms seen in association with catarrhal and purulent conjunctivitis and a form due to coalescence of phlyctenules.

Salomonsohn [3] in an isolated case report and Martin [4] in a report of 5 cases described a condition which seems to have resembled the condition described by Fuchs, which has a mild course and heals in four to fourteen days. In Wood's encyclopedia of ophthalmology [5] there is described the severe form of ring ulcer, with loss of the whole cornea

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1. Fuchs, E.: Text Book of Ophthalmology, translated by A. Duane, New York, D. Appleton and Company, 1893; cited by Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1928.

2. de Schweinitz, G. E.: Diseases of the Eye, ed. 8, Philadelphia, W. B. Saunders Company, 1916, p. 250.

3. Salomonsohn, H.: Deutsche med. Wchnschr. **25**:527, 1899.

4. Martin, W. A.: Ophth. Rec. **8**:176, 1889; **9**:395, 1900.

5. Wood, C. A.: The American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1914, vol. 5, p. 3440.

when it is surrounded by a deep ring of infiltration. Paracentesis and early use of the cautery when perforation threatens are advised. From Terlinck is quoted a case of severe bilateral involvement apparently due to the pneumococcus. There is no mention of the condition in the Schieck-Brückner handbook or in the textbooks of Axenfeld, Ball and Morax. Among many articles on trachoma one finds practically no consideration of this particular complication. Fuchs (sixth American edition, 1917) has a brief note on its occurrence in trachoma but without any emphasis on the prognostic significance of the ring form of infiltrate. MacCallan [6] did not mention ring infiltrate but made a statement regarding corneal vascularization which I consider significant. In cases of severe pannus, he stated, "The absence of the normal nutriment renders necessary the persistence of pannus vessels. It should not be interfered with, even though the visual acuity is depreciated. Such operations as pannus dissection [and] peritomy . . . are contra-indicated." Duke-Elder described the observations of Fuchs and gave a useful reference to zur Nedden's work.

Zur Nedden,[7] in his classical report on marginal ulcer, made some interesting observations. In 1902 and in 1904 he described a group of 76 cases of corneal ulcer, mostly of the marginal type, which occurred in the Rhineland near Bonn. In nearly all of these the small gram-negative bacillus which goes by his name was found. In 12 the marginal infiltration was so extensive as to involve all or nearly all the corneal periphery, and from his sketches the picture would seem to have resembled in many respects that in the second group of cases here described. In most of his cases no visible signs of conjunctivitis were present. In spite of this fact cultures of material from the conjunctiva as well as as from the ulcer were positive in cases in which the ulcer was typical and only in such cases. He stated the belief that the organism reaches the cornea from the conjunctiva but is pathogenic only for the cornea and produces no characteristic changes in the conjunctiva. This distinguishes the condition he described from the marginal ulcer known to occur in various forms of conjunctivitis, in which the infecting organisms are pathogenic for both the conjunctiva and the cornea. He expressed the opinion that other organisms may produce an identical picture of marginal keratitis with no visible conjunctival involvement. He mentioned that 2 of his patients had trachoma in the cicatricial stage but did not ascribe any significance to this.

The ulcer in most of his cases ran a rather benign course, healing in two to six weeks with the use only of atropine, heat and antiseptic collyriums and causing little loss of vision. This would distinguish his cases from the typical cases in this series, in which the central part of

6. MacCallan, A. F.: Trachoma, London, Butterworth & Co., Ltd., 1936, p. 33.
7. zur Nedden: Arch. f. Ophth. **54**:1, 1902; **59**:360, 1904.

the cornea was usually partially opaque and looked as though it would become necrotic. Zur Nedden reviewed various descriptions of marginal ulcer, and from his review it is apparent that Schmidt-Rimpler, Schweigger and Saemisch had seen patients with the severe acute form of ulcer with necrosis of the central part of the cornea. In the cases of Fuchs, however, the ulcer was more benign and corresponded more nearly to that in zur Nedden's cases. In the cases of other authors bacteriologic examinations were not reported as a rule or had given negative results. Zur Nedden's bacillus has not to my knowledge been described in cases of marginal ulcer outside the Rhineland.

Ellis [8] in 1939 reported 2 cases of superficial marginal punctate keratitis, in 1 of which, at least, the condition closely resembled that in the second group of cases to be reported. The patient, a man of 65, had marginal infiltrates which rapidly formed a complete ring, leaving the central portion of the cornea clear. Within four days this was also involved, and the eye was enucleated for relief of pain. During the next three years marginal infiltrates appeared on the other cornea, and that eye also finally came to enucleation. Sections showed infiltration of the anterior half of the cornea, most intense near the limbus. These are the only 2 eyes reported of which sections were studied. Apparently no bacteriologic examinations were made.

From this review it is evident that conditions which have answered to the name of ring ulcer or ring infiltration have varied greatly and have probably been due to different etiologic agents. The object of the present paper is to call attention to two special types of the condition, in which the integrity of the central part of the cornea is definitely threatened, and to the value of early keratotomy, which in my experience has entirely altered the prognosis for vision. These two types of the condition have in common the development of a ring of infiltrate which surrounds more or less completely the central portion of the cornea. This portion at first remains clear, but if the infiltrate is inadequately treated it rapidly becomes opaque, leaving a scar which greatly reduces vision.

The first type is that which occurs in trachoma. It is not seen in the early stages but appears only after pannus has developed to a considerable degree and in some cases after all active conjunctival lesions have healed. As the first stage of the condition a number of pinpoint infiltrates appear at the ends of the new-formed vessels. After any sort of irritation, including that of trichiasis or of too vigorous use of copper, these gray points appear almost simultaneously. They rapidly coalesce, forming a ring or a horseshoe-shaped gray line enclosing the nonvascular portion of the cornea. This line breaks down to form a shallow ulcer covered with gray exudate. If untreated the ulcer becomes deeper,

8. Ellis, O. H.: Am. J. Ophth. **22**:161, 1939.

and when the deeper layers of stroma are involved the whole enclosed area, its nutrition from the limbus vessels being cut off, becomes opaque. Perforation occurs rarely, and hypopyon is never seen. Bacteriologic examination usually gives negative results or reveals common saprophytes.

In Nebraska this was the only type of ring ulcer I ever encountered. It was seen in from 1 to 3 cases a year, and my father had learned to know its rapid course and bad prognosis. It was not uncommon to see the two eyes affected either simultaneously or at short intervals in cases of old and neglected involvement. He showed me the value of the radical method of treatment which will be described. In Chicago, where trachoma is rare, only 4 such cases have been noted in eleven years. These are described hereafter, case 1 being worth describing in detail.

CASE 1.—M. H., a man of 65, had contracted trachoma fifteen years before and had received treatment with copper and by expression. A year before I saw him

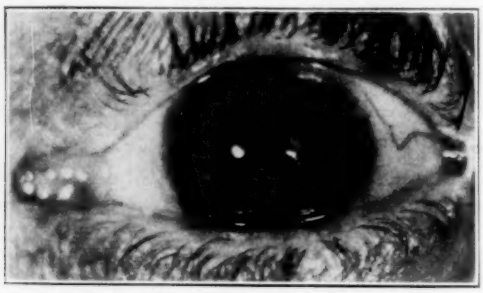

Fig 1 (case 1).—Ring ulcer in trachoma after ten months.

there developed on the right cornea an ulcer which had such a severe course that the eye was enucleated for pain. When I first saw him, on April 10, 1931, an ulcer which he said was exactly similar to the first one had been present in the left cornea for a week. The lids showed the picture of healed stage IV trachoma. The left cornea showed a typical horseshoe-shaped infiltrate enclosing an area of cornea not over 5 mm. in diameter. The horseshoe was open at the top for about 2 mm. but otherwise complete. The central area was already partially opaque, allowing vision of only hand movements. Examination of scrapings from the ulcer gave negative results. After the use of atropine sulfate and an application of optochin hydrochloride, a keratotomy was performed just central to the deepest area of ulceration, between 12:30 and 2 o'clock. The incision was reopened daily for ten days, during which time the central area cleared and the ulcer healed almost completely. The keratotomy wound was allowed to heal, but four days later an area of ulceration near 6 o'clock became active again. A second keratotomy was performed in this area, and the incision was reopened daily for fourteen days, the ulcer having shown no signs of activity for the last five days. Vision was 4/70 on dismissal and cleared within a month to 20/70. Clearing continued, and ten months after the original admission vision was 20/40 with correction (fig. 1). It remained approximately the same until the past year, when senile changes in the lens reduced it to 20/50. A few lashes were destroyed, and a small area of elevated epithelium

required a few applications of trichloroacetic acid; but no further ulceration had occurred, and the corneal vessels are now almost invisible.

CASE 2.—Mrs. H., aged 40, had the florid stage III of trachoma affecting the left eye. The other eye was in the healed, cicatricial stage. She was seen with Dr. Albert Hall in 1931. She had suffered from recurring corneal ulcers in both eyes for the past seven years. The right eye had been quiet for one year, but the left had been under treatment for the past few weeks. The infiltrates of the left eye had not completely coalesced, some still being discrete. Keratotomy was performed central to the deepest area of infiltration after application of trichloroacetic acid, and the incision was reopened daily for three days, at the end of which all the infiltration had healed. After three weeks the folds were expressed and treatment with copper was resumed. Vision returned to 6/10 after three months. In 1937, according to Dr. Hall's report, vision was 8/10 and no further ulcers had occurred.

CASE 3.—E. M., aged 44, showed a slightly different type of infiltrate. It began, as in the more common ulcers in trachoma, at the edge of the pannus but below the

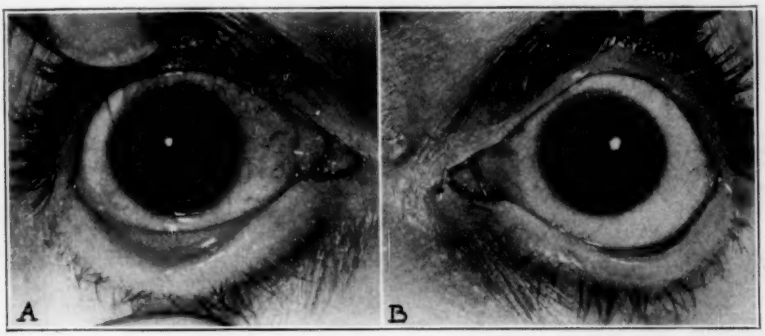

Fig. 2 (case 4).—Bilateral ring ulcer in trachoma after five years. *A*, right eye; *B*, left eye.

corneal center. Other infiltrates appeared below, however, outlining a shallow oval area in the lower third of the cornea. Keratotomy resulted in healing, with vision of 20/200. The patient was in the late third stage of trachoma. Two years later another severe ulcer developed at the same location, but this healed after early keratotomy without ever assuming the typical ring form.

CASE 4.—Rabbi G., seen with Dr. Beulah Cushman in 1937, presented bilateral ring infiltrates. He had been treated for trachoma since 1933 and had shown several small ulcers on each cornea during that time. He was in stage III, with marked pannus, especially in the left eye. This eye showed a ring infiltrate which was very near the center of the cornea because of the extensive vessels entering the cornea from all directions. The other eye had become involved a few days later and a week before I saw the patient. In this eye the ring was of the same type as that in the first case but entirely surrounded a clear central area. Pain and photophobia were intense and prevented reliable refraction. Keratotomy was performed by Dr. Cushman on both eyes. In the right eye the cut was made central to the deepest infiltrate, while in the left the central area was so small that a location just outside the ring was chosen. The chambers were reopened every day or every other day for three weeks, after which healing was complete. Vision five years later was 20/50 in the right eye and 20/100 in the left (fig. 2).

All these cases were observed in the presulfanilamide era. It seems likely that such cases will occur more rarely now that the employment of combined local and systemic therapy is common, although in the first case the ulcer occurred when all active trachoma was healed and there was no indication for sulfanilamide therapy. The most likely explanation of the occurrence of ulcer after the trachoma has healed seems to be that obliteration of the new-formed vessels proceeds too rapidly when the cornea is still dependent on their blood supply. The infiltrate would hence be due to points of focal necrosis which spread to form a ring of necrotic tissue. Sometimes areas of active trachomatous infiltration are evidently at fault.

The second type of ring infiltrate is seen during or just after an infection of the respiratory tract and in some cases without any previous illness. The patients in my experience have usually been young and

Fig. 3.—Marginal form of superficial punctate keratitis.

apparently healthy adults, although 1 was a woman of 63. The early picture corresponds in appearance to what Fuchs called metastatic marginal ulcer. As in the condition he described, the first stage is the appearance of multiple punctate infiltrates near the limbus (fig. 3). Cases in which this occurs are relatively common, and the condition usually heals without the development of a ring infiltrate. When the disease stops at this stage it may well be called by Fuchs's name, marginal superficial punctate keratitis. In a few cases, however, the infiltrates are especially numerous and close together and they rapidly fuse to form a more or less complete ring of infiltration. This is a much larger ring than that seen in trachoma, since it begins just in from the limbus. The prognosis is not so bad as in the trachomatous type, since the infiltration is closer to its blood supply and apparently heals spontaneously in some cases. In other cases, however, the ring deepens and the whole central area becomes rapidly opaque. The picture varies more than that seen in trachoma, and various etiologic agents may be responsible. Fuchs thought that bacteria reach the cornea through

the limbal vessels, and apparently they do in some cases. In others a virus infection like that of the more common form of superficial punctate keratitis is present. Bacteriologic examination has given negative results in my cases, except in 1, which will be described, and inoculations of the rabbit's cornea in several cases have produced no effect.

The most severe ring ulcer seen in a nontrachomatous person was that in case 5.

CASE 5.—Mrs. B., aged 63, during the past year had several attacks of conjunctival congestion lasting two to three days, but these had cleared up spontaneously. A week before her first visit she was awakened by pain in the left eye. She was treated by the family physician for several days with drops and injections of foreign protein and then by Dr. Elmo Dillon, who referred her to me on Jan. 3, 1941. Local applications of iodine had failed to affect the condition. Vision in the left eye was counting of fingers. A complete ring of infiltration and ulceration from 1 to 1.5 mm. wide was present. The central part of the cornea was dull and stained with fluorescein (fig. 4 *A*). Marked congestion, photophobia and pain

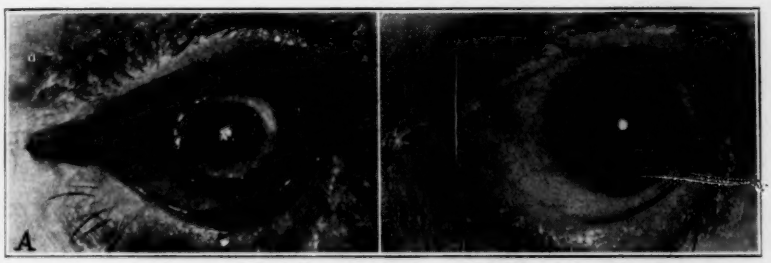

Fig. 4 (case 5).—Ring ulcer (second type). *A*, in active stage; *B*, one month later.

were present, but there were no signs of trachoma. Scrapings of the ulcer showed no bacteria, and inoculation of a rabbit's cornea with this material gave negative results. After application of iodine,[9] keratotomy was performed central to the deepest infiltrate from 12:30 to 1:30 o'clock. The patient was given large doses of vitamin A and for forty-eight hours enough sulfanilamide to establish a level in the blood of 11 mg. Administration of the sulfanilamide was stopped on account of fever and other symptoms. Three injections of typhoid vaccine were given by vein, with a moderate reaction. The keratotomy incision was reopened twice daily for two days and then once daily till January 23. A second, smaller keratotomy was done central to one of the lower infiltrates, and mercurochrome paste or iodine was applied daily to the ulcer. On January 24 the ulcer no longer stained and the chamber was not reemptied. The depression filled up, the eye became quiet and on January 30 vision was 6/24 (fig. 4 *B*). The central area continued to clear, and in April Dr. Dillon reported the vision to be 20/65 with correction.

On December 1 the patient returned with an exactly similar ring ulcer of the right cornea. Keratotomy was done the following day and the ulcer healed after

9. The following preparation of iodine was used in these cases: 5 grains (0.3 Gm.) of iodine, 5 minims (0.3 cc.) each of tincture of iodine and glycerin and 2 minims (0.12 cc.) of saturated solution of potassium iodide.

the chamber had been opened for three successive days. No chemotherapy or foreign protein therapy was employed.

CASE 6.—A. G., aged 18, was seen in 1938. A week before, when she was recovering from influenza, her left eye had become inflamed, and when I saw her she presented the picture seen in figure 5. Keratotomy was performed at

Fig. 5 (case 6).—Ring ulcer (second type) in active stage.

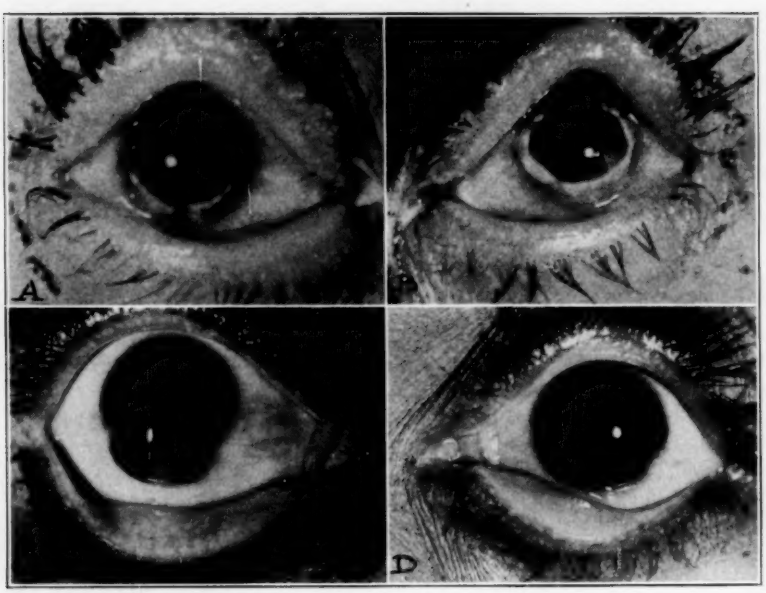

Fig. 6 (case 7).—Ring ulcer (second type). *A*, right eye in active stage; *B*, left eye in active stage; *C*, right eye two years later, and *D*, left eye two years later.

once after the application of iodine, and the incision was reopened daily for one week. Although later data are incomplete, her physician reported that the central part of the cornea became clear and that good vision was recovered.

CASE 7.—R. McC., a healthy Negro aged 22, was seen at Cook County Hospital. Both eyes had been inflamed for five months, but pain and loss of vision had progressed rapidly during the past week. The vision was 10/200 in the right eye and 5/200 in the left. The picture on admission is shown in figure 6 *A* and *B*.

Conjunctival scrapings showed gram-negative diplobacilli and a few staphylococci. In scrapings of the ulcers a number of staphylococci were found but only a few diplobacilli. The bacilli grew scantily on Löffler's medium, producing liquefaction, and hence may be considered Morax-Axenfeld bacilli. Keratotomy was performed on each eye by the resident, and the wounds were reopened daily. Prolapse of the iris occurred through the right keratotomy wound, apparently after reopening of the chamber; so the reopening was discontinued. Healing occurred after three weeks but with considerable central opacity, which had reduced the vision to 10/200 in the right eye and 12/200 in the left four months after admission. Two years later both corneas had cleared considerably (fig. 6 *C* and *D*). Vision in the right eye was 4/200 owing to irregular astigmatism, and the tension was 35 mm. (Schiötz). An iridectomy was indicated on account of the adherence of the iris, a complication which has not occurred in any other case. Vision in the left eye improved to 20/40 with correction.

Several conditions might from the name alone be confused with ring ulcer. There will be no confusion, however, in the mind of any ophthalmologist who has seen a typical lesion. Ring abscess is, of course, an entirely different condition, in which infection, usually through a perforating wound, has gained access to the interior of the eye and involves the posterior portions of the corneal periphery in a rapidly spreading purulent liquefaction. Marginal dystrophy of the cornea, unfortunately called by the Germans furrow keratitis, is a pure dystrophy which proceeds for years with little or no signs of inflammation, the corneal periphery gradually becoming thinner and occasionally showing small hernias of Descemet's membrane. The small erosions or ulcers which occur repeatedly along the arcus in older persons are superficial, produce only slight congestion and heal rapidly with or without applications of trichloroacetic acid. Mooren's ulcer is a chronic condition in which progress of the ulcer around and across the cornea is accompanied by vascularization and requires several months to cover the cornea, while in ring ulcer the ring is practically complete within a few days to a week. Catarrhal ulcer probably does form the beginning of ring ulcer in some cases, such as those of zur Nedden, and hence the indication exists for sterilization of catarrhal ulcers as early as possible. I have not, however, seen the usual type of catarrhal ulcer spread to form a typical ring, perhaps because of carrying out sterilization whenever possible.

THERAPY

As in the case of serpent ulcer, the most effective treatment must be given before the typical picture develops. There is, for some reason, a hesitancy on the part of some ophthalmologists to apply effective sterilizing agents to the cornea. It is true that many small infiltrations will heal without local applications, but it is also true that most of them will heal much more quickly when carefully controlled but adequate applications are made, while by such treatment the occasional severe sequelae of infiltrations which do not heal will usually be prevented. It has been my experience that conditions like that shown in figure 3,

with four to six infiltrates around the limbus, usually heal within two to three days when each infiltrate is touched carefully with pure trichloroacetic acid. The treatment may need to be repeated on one or two of the larger lesions or on new infiltrates which appear. The same is true of the isolated ulcers and small groups of infiltrates which appear in trachoma. Since the portions involved are out of the pupillary area there can be absolutely no objection to making such applications early rather than waiting for the development of a large confluent ulcer. In both conditions the use of atropine sulfate and the application of heat are part of the routine treatment, while applications to the palpebral conjunctiva of 2 per cent silver nitrate or 2 per cent zinc chloride may possibly be of value. The use of copper should be stopped on the appearance of ulceration in trachoma.

When a patient is seen with a well developed ring infiltrate, even if this does not quite surround the cornea the indication seems definite for decompression of the cornea by some means. Undoubtedly limbal paracentesis would suffice to bring about healing in a number of cases of early or of less severe infiltration. However, my experience with a form of keratotomy of which the incision can be reopened easily as often as necessary until complete healing of the ulcer has led me to favor it in such cases. The same principles are involved as in the delimiting keratotomy described by my father and familiar to most American ophthalmologists. Here, however, the incision can delimit only one portion of the ulcer, and it is found that when the decompression is repeated for a sufficient time the remainder of the ulcer heals. The cut need not be more than 3 mm. long and is placed just central to the most active portion of the ulcer. Anesthesia by injection of 4 per cent procaine hydrochloride solution, good fixation and use of a thin sharp Wheeler knife are as important as in delimiting keratotomy. It might seem that the location of the cut would favor prolapse of the iris, but this has occurred in only 1 of my cases and I feel sure it could have been prevented by proper technic. To avoid this danger it has been customary to delay the use of atropine until keratotomy has been performed, but the cut can be reopened after atropinization without any danger of prolapse. A Darling cystotome is an ideal instrument for this purpose. It is inserted just through the wound after the application of 2 or 3 drops of butyn sulfate or pontocaine hydrochloride and is turned enough to allow slow emptying of the chamber. Saturated iodine solution is usually applied to the ulcer before the chamber is opened or reopened, but this is not regarded as a really important part of treatment. It is considered important to reopen the incision daily or every second day until healing is complete. If signs of activity reappear at any point of the ring they indicate that healing was not complete and should be met by reopening the former incision, or, as in 2 of the present series, by making a new keratotomy incision central to the active area.

COMMENT

It is evident that ring ulcers of both the types here described are by no means rare, in spite of the lack of special attention paid to them in the literature. In trachoma there seems no doubt as to the specific causation, while in the second type described it is likely that a number of pathogenic agents are responsible in individual cases. These agents include zur Nedden's bacillus, the Morax-Axenfeld diplobacillus and probably other bacteria present on the conjunctiva. They probably also include a virus which causes superficial punctate keratitis of the marginal type, in which no ordinary bacteria are found. The difficulty of obtaining material for bacteriologic study from a relatively small lesion mostly beneath the corneal surface has been emphasized by zur Nedden and may account for a number of negative reports. It is also true that more systematic bacteriologic study should have been made in most cases. Zur Nedden's explanation of the involvement of the particular portion of the cornea affected is in most respects satisfactory. According to this explanation organisms of little or no pathogenicity from the conjunctiva involve the cornea when they reach the zone favorable for their growth. This is not the extreme corneal periphery, which is well nourished from the limbus vessels and is usually spared. The zone just central to it, where nutrition is less abundant, is affected. In the case of organisms pathogenic for the conjunctiva, conjunctivitis usually precedes the appearance of corneal lesions. In trachoma, it may be added, the zone involved is necessarily farther central, near the ends of the new-formed vessels and hence close to the important pupillary area. The unfortunate coincidence of several factors would seem to be responsible for the formation of the complete or nearly complete ring-shaped conformation of the ulcer, which changes a relatively benign condition to one involving great danger to the central part of the cornea. In trachoma the distribution of new vessels in the cornea is of most importance. In a patient with the customary pannus of the upper portion alone a ring infiltrate will never develop. Only when vessels are present all around the cornea and numerous infiltrates occur simultaneously at the ends of these will a ring ulcer develop. What factor touches off the development of all these infiltrates at once remains unknown.

In the second type of ring ulcer the number of infiltrates which appear is undoubtedly the most important factor, as these must be fairly close together in order to form a ring. It almost seems that a spastic contraction of already diseased capillaries must occur in some cases to cause the rapid development of the symmetric areas of necrosis. Perhaps this is the reason for the more frequent occurrence of the severe types of ring ulcer in persons past middle age, which has been described by other authors though it was not evident in this small series of cases.

WATER MOVEMENT AND THE EYE

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The object of this investigation was to determine the rate at which water enters and leaves the eye and, more particularly, to discover the rate of total water movement between the aqueous and its environment. To accomplish this, it is essential to distinguish one molecule of water from another, for water molecules in the eye are continuously exchanging with those in the blood stream, irrespective of any net flow. Because so-called heavy water (D_2O) cannot be distinguished physiologically from ordinary water, it is ideally suited for following the course of water molecules in biologic materials.

In the absence of any means of labeling the water molecules, all previous investigators of ocular fluid dynamics have been limited to measuring the net flow of liquid. It will be shown subsequently that the net flow represents but a small fraction of the total water movement within the eye; the total movement to the best of our knowledge has never been determined heretofore.

Provided there is no change in intraocular pressure, measurement of water movement into the eye and out of the eye should give identical results. In the present study an attempt was made to measure the water movement in the two directions and later to compare the results obtained. Thus the experiments fell into two general divisions: first, those in which measurements were made of the tracer (D_2O) entering the eye from the blood and, secondly, those in which the tracer left the eye. The first group was thought to be the more physiologic because the eye remained untouched throughout the period of the water movement. The measurements made in this way were considered satisfactory for movement of water into the aqueous, vitreous and lens. The second group of experiments was concerned with the rate of loss of D_2O from the eye to the blood. The substantial agreement of the data obtained by substituting D_2O for aqueous and those obtained when the eye was not so disturbed contraverts the possible objection that this preliminary

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manipulation upsets the normal ocular physiology. Notwithstanding the somewhat different types of data obtainable with each approach, it was possible to make a semiquantitative comparison of the results derived with the two experimental methods.

METHODS AND PROCEDURE

The successful use in animals of D_2O as a tracer substance for water depends on the fact that its diffusion rate is practically identical with that of ordinary water and yet its density is about 10 per cent greater. Thus the proportion of D_2O in any mixture with H_2O can be calculated from the specific gravity of the mixture, and the water movement may thereby be followed by determining either the rate at which D_2O is diluting ordinary water or by the converse of this. Since any foreign material would alter the specific gravity of such a mixture, it is necessary to eliminate completely all extraneous substances before determining the specific gravity. In the present experiments this was accomplished by combining the technics of Hevesy and Jacobsen [1] and Linderstrøm-Lang, Jacobsen and Johansen.[2]

In brief, the resultant method consisted in distilling off all the water and D_2O from the material whose D_2O content it was desired to determine, e. g. aqueous, whole eye or serum. This was done under reduced pressure at room temperature in an all pyrex sealed system, one end of which was immersed in liquid air. A small amount of phosphorus pentoxide (P_2O_5) was placed in the system in order to remove any ammonia which might otherwise distill over with the water. The distillate was placed in a second, smaller pyrex tube with the addition of a few milligrams of sodium peroxide (Na_2O_2) and potassium permanganate ($KMnO_4$). The liquid was redistilled by gradually raising the temperature of one end of the tube to about 120 C., the fluid condensing meanwhile at the other end. After this second distillation the tube was tilted so that the water mixture would run back into the end from which it came, and the process was carried out twice more.

The specific gravity of the resultant distillate was then determined by means of a Linderstrøm-Lang constant density gradient tube. For the present experiments a gradient tube was constructed having a sensitivity sufficient to differentiate an absolute amount of D_2O corresponding to 1 part in over 2,000 parts of water (less than 0.05 per cent).

To test the adequacy of the method, samples of 1 per cent sodium chloride solution, rabbit aqueous, serum and lens were distilled separately in the manner outlined, and the specific gravities of the distillates were found to be indistinguishable from the specific gravity of distilled water; i. e., the distillates contained less than 0.05 per cent of D_2O.

1. Hevesy, G., and Jacobsen, C. F.: Rate of Passage of Water Through Capillary and Cell Walls, Acta physiol. Scandinav. **1**:11-18, 1940.

2. Linderstrøm-Lang, K.; Jacobsen, C., and Johansen, G.: On the Measurement of the Deuterium Content in Mixtures of H_2O and D_2O, Compt. rend. d. trav. du Lab. Carlsberg, série chim. **23**:17-25, 1938.

A second set of control experiments was performed to check the accuracy of the recovery of D_2O from serum. Since the greatest errors would be expected to occur with low absolute concentrations of D_2O, sufficient of this material was added to serum to correspond to but 0.60, 0.30 and 0.15 per cent of the total water content. The recoveries in duplicate were as follows: 0.59 and 0.59, 0.33 and 0.33, and 0.19 and 0.18 per cent, respectively. From these results it will be seen that all values corresponded to within an absolute variation of less than 0.05 per cent of D_2O, and since in practice absolute concentrations were usually above 0.50 per cent of D_2O, the error so involved was less than 10 per cent in any single experiment.

The procedure adopted for the "blood to eye" series of experiments consisted in injecting intraperitoneally into small, unanesthetized rabbits about 10 cc. of 50 per cent D_2O made isotonic with sodium chloride. The intraperitoneal route was chosen for the speed and ease with which the injection could be carried out in small rabbits and also because the concentration of D_2O in the blood was found to be more constant than when the intravenous route was used. Samples of aqueous were withdrawn with the animals under topical anesthesia with pontocaine hydrochloride. When samples of vitreous were desired the animal was killed by decapitation, the eye was enucleated immediately and the vitreous was withdrawn from the back of the eye with a syringe. Samples of blood were obtained either by puncture of the heart or from an ear vein. All time intervals were considered to start when half of the fluid had been injected and to end when the sample to be tested was taken.

The procedure used for the "eye to blood" set of experiments at first included preliminary anesthetization with soluble pentobarbital U. S. P. (pentobarbital sodium) in addition to the local application of pontocaine hydrochloride. The barbiturate was omitted from about half of the experiments with no apparent effect on the results. With or without general anesthesia aqueous was withdrawn into a syringe and, the needle not being removed from the eye, a second syringe, carefully calibrated, containing D_2O made isotonic with sodium chloride, was attached to the needle and approximately the same quantity of fluid was restored to the eye. On the average the exchanged quantity of liquid represented about 80 per cent of the calculated total volume of aqueous. A correction of 0.02 cc. was made for loss of D_2O in the needle. The needle (no. 27) was then cut with a dull pair of cutting pliers in such a way that the cut end was simultaneously sealed against leakage of aqueous. The end of the needle was left projecting through the cornea. The advantage of this technic is twofold. First, it leaves the experimenter free to kill the animal and enucleate the eye or to perform the second paracentesis with an uncontaminated needle. Secondly, it prevents leakage which would arise otherwise from distortion caused by holding a syringe against the rabbit's eye. That this method did actually prevent leaks around the needle was demonstrated by the absence of dilution of 2 per cent fluorescein solution placed on the cornea at the point of penetration by the needle.

The next step in the procedure consisted either in withdrawing aqueous again or in enucleating the eye for a single analysis or for analysis of the lens and of the vitreous separately. In the experiments in which no general anesthetic had been given, the animal was first killed instantaneously by decapitation.

Since the weight of the eye was always determined, whereas the volume of the aqueous was not usually measured, the actual starting concentration of D_2O in the aqueous was calculated from the experimentally determined aqueous to whole eye ratio of 0.095. For the experiments involving the whole eye, a 90 per cent moisture content was considered normal for calculating the amount of D_2O left in the eye from the experimentally determined concentration.

RESULTS

The results obtained from the injection of D_2O into the peritoneal cavity of 4 rabbits are shown in table 1. From the data on rabbit 1 it

TABLE 1.—*Measurements of the Total Water Movement from Blood to Aqueous, Vitreous and Lens*

Rabbit *	Time, Min.	Concentration of Deuterium Oxide: Blood, Percentage	Aqueous, Percentage	Vitreous, Percentage	Lens, Percentage
1	0	0	0	0	.....
	6.5	.....	0.45 left eye	.....	.....
	15.3	0.85	.....	.....	.....
	17	.....	0.76 right eye	.....	.....
	26.8	0.87	.....	.....	.....
	93	0.89	.....	.....	.....
	1,688	0.80	.....	.....	.....
	1,700†	.....	0.82 both eyes‡	0.79 both eyes	.....
2	0	0	0	0	.....
	5.9	.....	0.25 left eye	.....	.....
	8.4	0.56	.....	.....	.....
	11.4	.....	0.32 right eye	.....	.....
	13.8	0.56	.....	.....	.....
	33	0.51	.....	.....	.....
	4 days†	0.20	0.20 both eyes‡	0.20 left eye 0.20 right eye	.....
3	0	0	0	0	0
	3.5	.....	0.44 left eye	.....	.....
	3.7†	1.27	0.43 right eye	0.10 left eye 0.13 right eye	0.07 left eye 0.10 right eye
4	0	0	0	0	0
	1.5	0.52	.....	.....	.....
	2.7	0.81	.....	.....	.....
	6.7	0.81	.....	.....	.....
	9.7	.....	0.66 left eye	.....	.....
	10.1†	0.81 0.81	0.66 right eye	0.26 left eye 0.26 right eye	0.22 left eye 0.22 right eye

† Animal killed.
‡ Secondary aqueous.
* D_2O was injected intraperitoneally as follows: rabbit 1 (weight 660 Gm.), 10.0 cc. of 55 per cent D_2O; rabbit 2 (weight 800 Gm.), 7.75 cc. of 55 per cent D_2O; rabbit 3 (weight 780 Gm.), 8.0 cc. of 80 per cent D_2O, and rabbit 4 (weight 1,300 Gm.), 8.0 cc. of 80 per cent D_2O.

may be seen that D_2O enters the blood stream and that the proportion of D_2O in the aqueous soon approaches that in the blood. Had the concentration of D_2O in the blood been at a constant level throughout the test period, the exact half-life [3] of water in the aqueous could

3. A term used hereafter to designate the time necessary for half the water content of the eye or of a part of the eye to be replaced with new water. This unit is made necessary from the fact that it is meaningless to speak of the time necessary for all the water to be replaced, because theoretically an infinite time is required.

readily have been calculated. In the absence of this ideal situation and more especially in the absence of any exact knowledge about the rate of change of blood D_2O content, it is justifiable only to state that after 15.3 minutes the ratio of D_2O in the aqueous to that in the blood was about 0.90. However, it is possible that the aqueous may have reached this proportion even more rapidly. Thus the half-life of 4.25 minutes calculated from this ratio represents a maximum period. It is noteworthy that the vitreous as well as the aqueous of rabbit 1 was indistinguishable from the blood with respect to its D_2O content when measured at twenty-eight hours.

Also shown in table 1 are the findings from 3 similar experiments. It will be observed that these data are consistent with those on rabbit 1. The half-life of the aqueous from rabbits 2, 3 and 4 is found by calculation to be less than 7.2, 6.0 and 4.0 minutes, respectively. From the data shown for the third and fourth experiment, the maximum half-life period for water in the vitreous is similarly found to be less than 26 and 16 minutes, respectively. The calculated value is based on the assumption that all the water is coming from the blood. The truth of this assumption will be demonstrated later in this paper. It is interesting to note that if a ratio of vitreous volume to aqueous volume of 7 is taken as being approximately correct for the rabbit, the absolute quantity of water moving into the vitreous is calculated from rabbits 3 and 4 to be approximately one and seven-tenth times that moving into the aqueous. While for obvious reasons this ratio must be considered only approximate, it should be pointed out that the same variables which limit the calculation of half-life periods to maximum periods are simultaneously affecting the vitreous as well as the aqueous. When one is calculating the ratio of the absolute amount of water movement in any two parts of the eye, the variables cancel out, so that the ratio does not involve a comparison of two unknowns.

The data on rabbits 3 and 4 also illustrate the fact that there is appreciable water exchange between the lens and its environment. Unlike the aqueous and the vitreous, however, the immediate source of water for the lens is not the blood stream. Thus it is not possible to arrive at a comparable half-life period of the water in the lens from the data reported.

As stated before, the second group of experiments consisted in replacing a portion of the aqueous with D_2O, and, after various times, determining the concentration of D_2O remaining in the whole eye. The results obtained from performing 19 such experiments on rabbits are shown in chart 1. From the line made up of solid circles in this chart, it will be seen that the percentage of D_2O remaining in the eye when plotted on a logarithmic scale decreases linearly with time for the first 7 to 8 minutes and thereafter appears to decrease somewhat less rapidly.

This means that the amount of D_2O leaving the eye is simply dependent on the amount present for the first 7 to 8 minutes, but thereafter the amount of D_2O leaving the eye is considerably less than would be expected on this basis. The deviation from linearity may be explained on the assumption that an appreciable proportion of D_2O is by this time forming an equilibrium within the eye itself, viz. with the lens and the vitreous. Data to be presented later support such an assumption. Unfortunately this secondary equilibrium, tending to slow down the rate of loss of D_2O from the eye, makes any calculation of the half-life of water in the aqueous slightly too long. From chart 1 the approximate half-life may be read directly; it is 3.6 minutes.

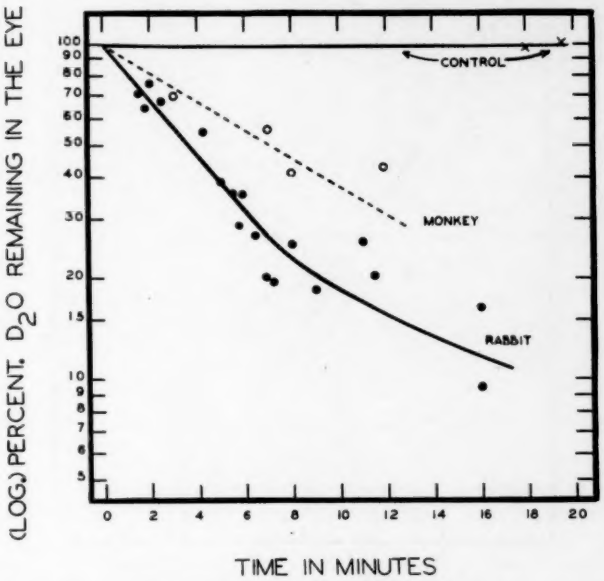


Chart 1.—The percentage of D_2O remaining in the whole eye at various intervals after replacement of part of the aqueous with a known amount of D_2O.

The line made from the crosses in chart 1 represents 2 control experiments performed on eyes in situ of dead animals. The high proportion of recovered D_2O after about 20 minutes shows that the loss of D_2O from eyes of living animals appears to be associated with the blood stream and that no appreciable proportion is lost by diffusion through the globe. Moreover it again demonstrates the adequacy of the methods involved.

The broken line of chart 1 shows the results from similarly conducted experiments on the eyes of 2 monkeys (Macacus rhesus). The approximate half-life of water in the aqueous appears to be less than 7.0

minutes. The accuracy of this result is, of course, limited by the small number of measurements. It does appear probable from these results, however, that the half-life of the water in the aqueous of the monkey is longer than that in the aqueous of the rabbit.

In an attempt now to determine the half-life of water in the aqueous of rabbits, diffusion into the other parts of the eye being taken into consideration, D_2O was substituted for part of the aqueous as in the experiments just discussed, but, instead of analysis of the whole eye for D_2O after varying intervals, the percentage of D_2O remaining in

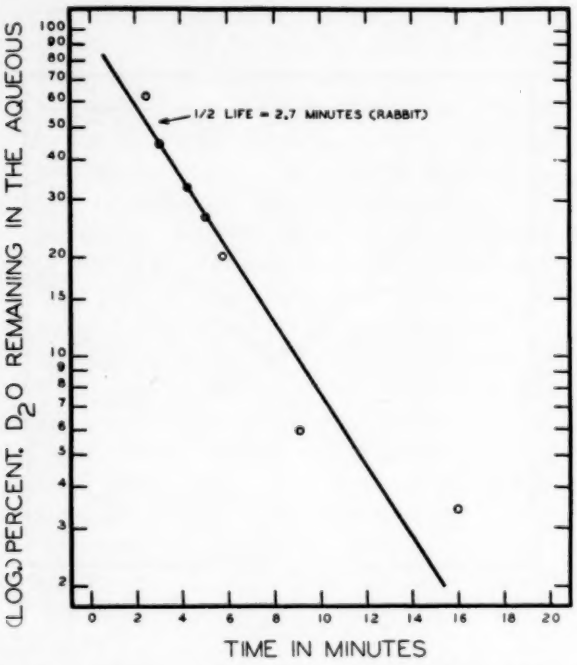


Chart 2.—The percentage of D_2O remaining in the anterior chamber at various intervals after replacement of part of the aqueous with a known amount of D_2O.

the aqueous was determined directly. In order that all the experimental results might be comparable, the initial concentrations of D_2O were mathematically adjusted to 100 per cent and the final concentrations were proportionately increased. This obviously has the additional advantage that all quantitative relationships so established are identical with the actual total water movement.

The results of 7 experiments conducted in this manner are depicted in chart 2. The half-life of the water in the aqueous is seen to be 2.7 minutes. From the fact that the results appear to be best represented

by the straight line shown in the chart, it is possible to state that the proportion of D_2O leaving the aqueous to that present at any given time is a constant. In the light of this fact, the deviation from a straight line of the logarithm of the concentration of D_2O remaining in the whole eye, as shown in chart 1, must indeed be caused by the assumed secondary equilibrium within the eye itself.

Direct experimental evidence which substantiates this assumption is presented in table 2, where the amount of D_2O which is exchanging with ordinary water from the lens and from the vitreous is shown. Here it may be seen that the ratio of the amount of D_2O in the lens and in

TABLE 2.—*Deuterium Oxide Movement from Aqueous to Vitreous and Lens* *

Rabbit Eye	Time Min.	Aqueous D_2O Percentage	Aqueous D_2O Mg.	Vitreous D_2O Percentage	Vitreous D_2O Mg.	Ratio: Amount of D_2O in Vitreous to That in Aqueous	Lens D_2O Percentage	Lens D_2O Mg.	Ratio: Amount of D_2O in Lens to That in Aqueous
				Living Eye in Situ					
1	0	31.2	80.0	0	0	.....	0	0	.....
	4.3	10.3	26.5	.....	.....	.....	.....	.....	.....
	6.0	.....	.....	0.10	1.8	0.068	1.2	3.2	0.12
2	0	29.0	80.0	0	0	.....	0	0	.....
	5.0	7.8	21.5	.....	.....	.....	.....	.....	.....
	7.0	.....	.....	0.05	1.0	0.047	0.90	2.6	0.12
3	0	35.0	90.0	0	0	.....	0	0	.....
	16.0	1.2	3.1	.....	.....	.....	.....	.....	.....
	19.0	.....	.....	0.10	1.8	0.58	0.70	1.9	0.61
				Enucleated Eye					
4	0	42.0	104	0	0	.....			
	5.5	25.5	63	0	0	0			
5	0	40.0	100	0	0	.....			
	10.0	22.4	56	0.13	2.3	0.041			

* Accuracy of D_2O determinations, ± 0.025 per cent.

the vitreous to the amount left in the aqueous increases with time. Particularly does this appear to be true after 7 minutes, for between 7 and 19 minutes the ratio increases about twelvefold and fivefold for the vitreous and for the lens, respectively. It is clear from table 2 that this increase is caused not by a great increase in the absolute D_2O concentration in the vitreous and in the lens but by the fact that the concentration in the aqueous has by this time decreased so considerably through loss to the blood stream. The findings from similar experiments conducted on enucleated eyes are also shown in table 2. Here the amount of water exchanging between the aqueous and the vitreous is shown to be approximately the same as in the living eye.

An attempt was made to obtain comparable data for the vitreous of the living eye by introducing the D_2O into this structure. Since one could not withdraw vitreous and still maintain a leak-proof scleral-needle

junction when the D_2O was introduced, a small amount of 80 per cent D_2O (0.07 cc.) was injected without the previous withdrawal of any vitreous. As was to be expected, the pressure within the eye was greatly increased. Analysis of the aqueous after 11 minutes showed that none had gone into the anterior chamber, and analysis of the whole eye showed that less than 0.25 per cent had left the eye in this period. It appears that the increased intraocular pressure abolished the usual water exchange between the blood and the eye.

In table 3 are summarized all the results pertaining to the half-life periods of the water in the aqueous and the vitreous. There is general agreement among the results obtained from the several different approaches.

TABLE 3.—*Summary of Half-Life Periods of the Water in the Aqueous and Vitreous as Determined by Several Methods*

Measured from	Half-Life Minutes	No. of Experiments
Rabbit Aqueous		
Blood to aqueous	* Less than 4.25 ; 7.2 ; 6.0 ; 4.0	4
Aqueous to blood	* Less than 3.6 (average)	19
Aqueous to remainder of eye and blood	2.7 (average)	7
Rabbit Vitreous		
Blood to vitreous	* Less than 26 ; 16	2
Calculated †	About 11	2
Monkey Aqueous		
Aqueous to blood	* Less than 7.0	4

* See text.

†Calculated from a ratio of water movement into vitreous to that into aqueous of 1.7 and from the aqueous half-life period of 2.7 minutes.

COMMENT

It may not be at once apparent why more direct measurements were not made of the exact half-life periods of ocular water. However, it is not always technically possible to obtain a valid figure for many of these desired periods. For example, the value for the effective half-life of the water in the whole eye could not be measured by introducing D_2O into the blood and determining the subsequent D_2O content of the whole eye because of the misleading effect of an indeterminable amount of D_2O in the vascular bed of the eye. Neither could the value be ascertained by the reverse approach, because no practical method was available for obtaining a uniform concentration of D_2O throughout the whole eye to start with. Instead, then, the half-life of aqueous and of vitreous water alone had to be measured by the "blood to eye" approach and the half-life of the aqueous water alone by the "eye to blood" method.

Within the limitations cited it would appear that one half of the water in the aqueous is renewed every 2.5 to 3 minutes in the rabbit,

the great majority of the new water coming from the blood stream. This would be equivalent to approximately 50 cu. mm. per minute. It should be emphasized that this figure refers only to the water and may not apply to the other constituents of the aqueous.

Because of the few experiments performed on the vitreous, the total movement of vitreous water cannot be estimated with the same probable accuracy as that of the aqueous, but the order of magnitude is about 85 cu. mm. per minute in the rabbit.

It is interesting to compare the total water movement into or out of the anterior chamber with the so-called rate of formation of aqueous; the latter appears to be essentially the net flow of fluid through the anterior chamber. This is what previous investigators have measured in studying fluid exchange. They did this first by determining the flow of aqueous out of the eye, either after the intraocular pressure had been reduced or when the normal exit channels for aqueous had presumably been blocked, and secondly, by determining the rate of disappearance of substances injected into the anterior chamber, e. g. dyes. Both of these technics, unfortunately, have necessitated considerable departure from physiologic conditions. For this reason it is not astonishing to find that the rate so determined varies between 1 and 50 cu. mm. per minute. In general the more refined the technic the slower has been the reported rate of aqueous formation. Thus Friedenwald and Pierce,[4] who also reviewed the earlier literature, found that the rate of flow of aqueous is but 1 cu. mm. per minute. When this rate is used for comparison, the total water movement appears to be about fifty times the actual net flow of aqueous fluid. It would appear that a large part of the total water movement consists of water in the blood exchanging for water within the eye. Such reactions are probably simply expressions of the kinetic energy of the molecules involved. These findings are in complete agreement with the more recent concepts of the dynamic state of all the body constituents.

SUMMARY

The movement of water into and out of the eye has been measured by using D_2O as a tracer substance for water.

One half of the water in the aqueous of the rabbit was found to be replaced every 2.7 minutes. This corresponds to a total water movement into or out of the anterior chamber of approximately 50 cu. mm. per minute.

In a much smaller number of experiments one half of the water in the vitreous of the rabbit was calculated to be replaced every 10 to 15

4. Friedenwald, J. S., and Pierce, H. F.: Circulation of Aqueous: I. Rate of Flow, Arch. Ophth. **7**:538-557 (April) 1932.

minutes. This value would correspond to a total water movement into or out of the vitreous of approximately 85 cu. mm. per minute.

One half of the water in the aqueous of the monkey was found to be replaced in less than 7 minutes. This would correspond to a total water movement into or out of the anterior chamber of more than 13 cu. mm. per minute.

The quantity of water going from the aqueous to the vitreous and the lens of the rabbit was found to represent but a small portion of the total water movement out of the aqueous.

The rate of total water movement into or out of the aqueous is about fifty times as great as has recently been reported for the so-called rate of flow of whole aqueous.

CARBAMINOYLCHOLINE CHLORIDE IN THE TREATMENT OF GLAUCOMA SIMPLEX

C. S. O'BRIEN, M.D.
AND
K. C. SWAN, M.D.
IOWA CITY

Carbaminoylcholine is one of a group of synthetic choline derivatives which act principally by parasympathetic stimulation. In chemical structure (chart 1) it is similar to acetylcholine, but its action is more prolonged, since it is stable in the tissues and hydrolysis is slow.

The initial experiments on the ocular effects of carbaminoylcholine chloride were made on isolated iris sphincter and indicated that this drug may be the most powerful of all known miotics.[1] However, clinical reports have been conflicting. Guyton [2] in a recent review of the literature found no unanimity of opinion regarding the degree and the duration of miosis but concluded that the miosis is probably greater but less prolonged than that produced by similar concentrations of pilocarpine. Velhagen [3] found the effect of a 0.75 per cent concentration of carbaminoylcholine chloride on the accommodation of the normal human eye to be less than that of a 2 per cent concentration of a pilocarpine salt but reported no quantitative data.

Carbaminoylcholine chloride is known to be a powerful peripheral vasodilator, and Duke-Elder [4] has suggested that its effect on the ocular vessels might contraindicate its use in the treatment of acute congestive glaucoma. The only vascular reaction actually observed in the human eye has been a mild conjunctival hyperemia.[5] As experimental evidence

From the Department of Ophthalmology, State University of Iowa College of Medicine.

Read at the Seventy-Seventh Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 30, 1941.

The carbaminoylcholine chloride (doryl) for this study was supplied by Merck & Co., Inc. Zephiran was supplied by the Alba Pharmaceutical Co.

1. Velhagen, K., Jr.: Arch. f. Augenh. **107**:319, 1933.

2. Guyton, J. S.: Pharmacodynamics of Intraocular Muscles, Arch. Ophth. **24**:555 (Sept.) 1940.

3. Velhagen, K., Jr.: Klin. Monatsbl. f. Augenh. **92**:472, 1934.

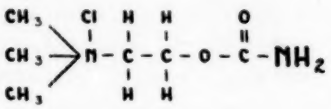
4. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3396.

5. de Sanctis, G. E.: Ann. di ottal. e clin. ocul. **65**:25, 1937.

that carbaminoylcholine chloride does affect the intraocular vessels, Swan [6] found that there was an elevation of temperature in the anterior segment of the eye, indicating an increased blood flow in the vessels to the iris and to the ciliary body. In studies with fluorescent dyes, Swan and Hart [7] observed that the drug had a greater dilating effect on the iris vessels than did other miotics. In other studies these authors reported that it increased the permeability of the blood-aqueous barrier to a greater extent than pilocarpine but to a lesser extent than physostigmine.

The hypotensive action of carbaminoylcholine chloride on the intraocular pressure was recognized by Velhagen [1] in 1933. A few additional reports have appeared in the foreign literature indicating that it might be a valuable drug in the treatment of glaucoma simplex.

CARBAMINOYLCHOLINE



ACETYLCHOLINE

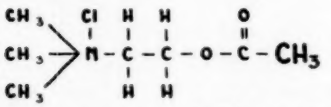


Chart 1.—Chemical structure of carbaminoylcholine chloride.

Miloro,[8] Hynie [9] and de Sanctis [5] found that in 0.75 per cent concentration it was more effective in some cases than a 1 to 2 per cent concentration of a pilocarpine salt, while Magitot [10] and Wilenkin [11] observed that it had approximately the same effect as pilocarpine. No comprehensive study has appeared in the American or the British literature.

The permeability of the cornea to carbaminoylcholine chloride has not received attention, although Molitor [12] observed that the miotic

6. Swan, K. C.: To be published.
7. Swan, K. C., and Hart, W. M.: Am. J. Ophth. **23**:1311, 1940.
8. Miloro, A.: Ann. di ottal. e clin. ocul. **63**:780, 1935.
9. Hynie, J.: Seskoslov. ofth. **2**:245, 1935.
10. Magitot, A.: Bull. Soc. d'opht. de Paris, 1939, p. 38.
11. Wilenkin, M.: Klin. Monatsbl. f. Augenh. **96**:84, 1936.
12. Molitor, H.: J. Pharmacol. & Exper. Therap. **58**:337, 1936.

effect of choline derivatives on the cat's eye varied with the method of administration, and Swan and Hart [7] reported that carbaminoylcholine chloride was not consistently absorbed through the rabbit's cornea unless the cornea was massaged. The permeability of the human cornea to carbaminoylcholine chloride has not been investigated, and the possibility of poor absorption has not received attention in previous investigations. Differences of opinion regarding the degree and the duration of the drug's action have indicated that some such factor is involved.

The present study was undertaken to determine the clinical effects of carbaminoylcholine chloride on normal and on glaucomatous eyes, the factor of absorption being taken into consideration.

TABLE 1.—*The Absorption of Aqueous Solutions of Carbaminoylcholine Chloride as Affected by Induced Changes in the Corneal Epithelium*

Treatment of Cornea	Average Concentration Producing Complete Miosis After Single Instillation (0.05-0.08 Cc.)	
	Treated Eye	Control Eye
Corneal massage		
Pipet tip—rabbits	0.09%	3-5%
Through lids—human beings	0.09%	1.5-4.5%
Corneal abrasion needle—rabbits	0.05%	3-5%
Drying of corneal surface by exposure—rabbits	0.06%	3-5%
Topical anesthetics (pontocaine hydrochloride, phenacaine hydrochloride and butyn sulfate)		
Rabbits	0.06%	3-5%
Human beings	0.06%	1.5-4.5%
Detergents—rabbits	0.06%	3-5%
0.1% zephiran, 1.0% saponin (Mallinckrodt), 0.1% duponol PC, 0.1% aerosol OT (100% pure)		
Buffer solutions—rabbits, p_H 2.8 and p_H 9.2	0.08%	3-5%

Studies of the permeability of the cornea to aqueous solutions of the drug were made on human volunteers and on rabbits. In these experiments an amount of aqueous solution just sufficient to cover the cornea (0.05 to 0.08 cc.) was taken as the standard dose, and the concentration of the solution was varied until the minimal concentration was found which would produce a maximal degree of miosis under standard conditions of illumination. In human beings, if the corneal epithelium was not disturbed the miosis was extremely variable in onset, degree and duration, and in several patients there was no change in the size of the pupil. Disturbing the corneal epithelium by massage, abrasion, drying or application of chemical agents had a pronounced effect on absorption, and the effectiveness of aqueous solutions of the drug in human beings and in rabbits could be increased fifty to seventy-five times by such procedures (table 1).

The chemical and the physical properties of carbaminoylcholine chloride explain the lack of corneal permeability to it. It is a lipid-insoluble, surface-inactive, polar compound. Unlike the alkaloids commonly used in ophthalmology, it does not become a lipid-soluble, free base at any p_H.[13] Cellular physiologists have long known that substances with these properties do not enter living cells readily but that penetration is enhanced by the presence of surface tension–reducing substances. Therefore, the use of a surface tension–reducing agent in noninjurious concentrations was investigated as a possible means of increasing corneal permeability to the drug. Zephiran, a mixture of high-molecular alkyl, dimethyl and benzyl ammonium chlorides, was the detergent selected. It has had trial as an ocular antiseptic [14] and has been reported to have no effect on the corneal epithelium of animals in concentrations of 0.02 to 0.03 per cent.[15] When stronger concentrations were used (0.04 to 0.05 per cent) several cases of superficial punctate disturbances of the epithelium were observed in the State University of Iowa ophthalmic clinic, but recovery was spontaneous when the drug was discontinued, and the condition did not recur when concentrations of 0.02 to 0.03 per cent were used.

Comparative studies of the effects of carbaminoylcholine chloride in aqueous solution and in zephiran solution were made on the eyes of 10 normal patients varying in ages from 12 to 72 years. A single drop of 1.5 per cent carbaminoylcholine chloride in an aqueous solution of 0.03 per cent zephiran was instilled over the cornea of the right eye and a single drop of 1.5 per cent carbaminoylcholine chloride in distilled water over the cornea of the left eye of each patient. Measurements of the horizontal diameter of the pupil were made in dim illumination with a pupillometer accurate to 0.5 mm. The results, as shown in chart 2, reveal a more rapid onset, a greater degree and a more prolonged duration of miosis with the zephiran solution. Spasm of accommodation in the eyes receiving the aqueous solution was inconstant and averaged less than 0.5 D., while spasm of more than 0.5 D. lasting from thirty-six to eighty-eight hours was present in each of the eyes receiving the zephiran solution.

Massage of the cornea through the lids was found to enhance the absorption of carbaminoylcholine chloride in zephiran solution. However, when the drug was used in aqueous solution, administration and massage by the average patient were found to be ineffective and undependable.

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13. Henderson, V. E., and Roepke, M. H.: Physiol. Rev. **17**:373, 1937.

14. Allen, J. H.: Personal communication to the authors. Thompson, R.; Isaacs, M. L., and Khorazo, D.: Am. J. Ophth. **20**:1087, 1937.

15. Maier, E.: J. Bact. **38**:33, 1939.

Carbaminoylcholine chloride has a strong odor but is practically tasteless. Both it and zephiran are stable at room temperature, and the former loses little of its potency through boiling. Samples of carbaminoylcholine chloride–zephiran remained pharmacologically active after being kept at room temperature for over a year.

A comparative study with pilocarpine solution and carbaminoylcholine chloride–zephiran solution was considered the best method of clinical evaluation. Pilocarpine nitrate was selected because in concentrations up to 2 per cent it has been one of the standard drugs used in the treatment of glaucoma simplex. However, it is ineffective in many cases and in others tends to lose effectiveness after prolonged administration. Moreover, the duration of its action is relatively short and it must therefore be instilled three to four times daily to maintain

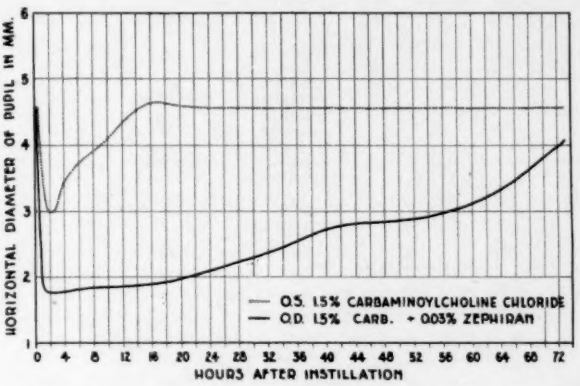
HORIZONTAL DIAMETER OF PUPIL IN MM.
6
5
4
3
2
1
O.S. 1.5% CARBAMINOYLCHOLINE CHLORIDE
O.D. 1.5% CARB. + 0.03% ZEPHIRAN
0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72
HOURS AFTER INSTILLATION

Chart 2.—The average effect of zephiran on the degree and the duration of miosis produced in 10 normal patients by single instillations of carbaminoylcholine chloride.

its maximum effect. Pilocarpine nitrate is absorbed readily, and zephiran enhances its action very little; consequently, it was used in aqueous solution.

Ten university students were used in the determination of the comparative effects of 1.5 per cent carbaminoylcholine chloride solution and 2 per cent pilocarpine nitrate solution on the normal eye. Each student received a single instillation of the pilocarpine solution in one eye and of the carbaminoylcholine chloride–zephiran solution in the other. Subjectively, the outstanding difference between the two drugs was the greater degree and the longer duration of blurring of distance vision produced by carbaminoylcholine chloride. This was accompanied by a greater degree of "aching" and "pull" in the eye. Objectively, spasm of accommodation was more intense and lasted much longer with this drug (table 2). The miosis which it produced was only slightly greater

than that produced by pilocarpine nitrate but lasted approximately three times as long (chart 3).

Comparative studies of the effects of carbaminoylcholine chloride and of pilocarpine were made on patients with chronic noncongestive glaucoma. The eyes of these patients were divided into two groups depending on the effectiveness of previous treatment with pilocarpine nitrate as judged by preservation of visual fields and lowering of intraocular tension.

In general the 14 eyes in which pilocarpine was effective represented early stages of the disease. The visual fields showed only minor defects,

TABLE 2.—*Stimulation of Accommodation Produced by Single Instillations of Carbaminoylcholine Chloride–Zephiran and Pilocarpine Nitrate Solutions*

Patient			Maximum Diopters of Myopia Produced *		Hours Required for Vision to Return to Normal	
Name	Age	Sex	Right Eye, 1.5% Carbaminoylcholine Chloride Solution in 0.03% Zephiran Solution	Left Eye, 2% Pilocarpine Nitrate Solution	Right Eye, 1.5% Carbaminoylcholine Chloride Solution in 0.03% Zephiran Solution	Left Eye, 2% Pilocarpine Nitrate Solution
K. S.	26	♂	2.12	1.00	69	11
M. P.	18	♂	1.12	0	38	0
J. E.	19	♂	1.87	0.87	62	6
H. D.	21	♀	0.87	0.37	56	3
R. B.	23	♀	0.87	0.62	39	7
F. L.	23	♂	0.62	0.37	46	2
E. W.	21	♀	0.87	0.37	42	5½
N. M.	21	♀	1.00	0.50	33	5
S. B.	20	♀	1.62	0.50	45	5
J. H.	22	♂	1.00	0.50	48	5½
Average	21.4		1.18	0.50	48	5

* Minus sphere added to previously determined cycloplegic correction to give maximum visual acuity.

corrected visual acuity was usually normal and on admission the tension with a single exception was less than 35 mm. mercury (Schiøtz). In 5 eyes, 1 per cent pilocarpine nitrate solution administered three times daily maintained the intraocular tension at a level slightly higher than that maintained by 0.75 per cent carbaminoylcholine chloride in zephiran solution administered twice daily, and with the former *intra diem* variations were greater. In 9 eyes, 2 per cent pilocarpine nitrate solution instilled three to four times daily was required to prevent loss of visual field. In 2 of these eyes the tension averaged 28 mm. of mercury in the early morning but there was no loss of field. In this group of eyes, tension was maintained an average of 5 mm. of mercury (Schiøtz)

lower by the administration of carbaminoylcholine chloride–zephiran solution two or three times daily.

The second group included 34 eyes with advanced glaucoma simplex. Only 14 of the 34 retained a corrected visual acuity of 6/9 or better, owing either to visual field defects involving the central area or to lens opacities. The visual fields determined on the Bjerrum screen revealed gross defects in all eyes but 1. In 6 eyes all but the central portion of the field had been lost. In 12 eyes peripheral areas of vision of varying size were retained but the fixation area was involved. Slit lamp microscopic examination usually revealed advanced changes in the anterior segment of the eye, e. g. obliteration of the temporal and of the nasal portion of the periphery of the anterior chamber, infiltration of the iris stroma with pigment, stromal atrophy, pathologic ectropion uvea and

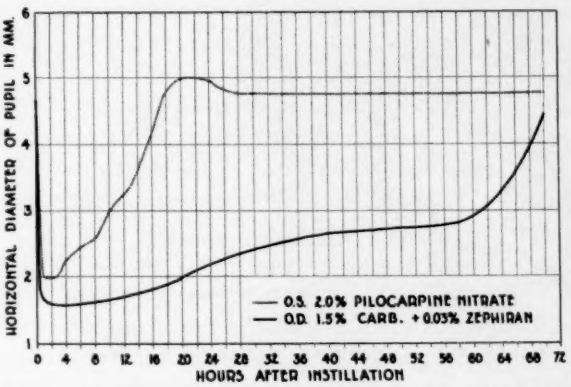
HORIZONTAL DIAMETER OF PUPIL IN MM.
1
2
3
4
5
6
0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72
HOURS AFTER INSTILLATION
O.S. 2.0% PILOCARPINE NITRATE
O.D. 1.5% CARB. + 0.03% ZEPHIRAN

Chart 3.—The average degree and duration of miosis in 10 normal adults following a single instillation of pilocarpine nitrate solution or carbaminoylcholine chloride–zephiran solution.

incipient cortical opacities. Ophthalmoscopic examination showed cupping, circumpapillary atrophy and some degree of pallor of the nerve head in almost every case. Many of the patients had advanced sclerosis of the retinal vessels. The average tension of this group of eyes on admission was 38 mm. of mercury (Schiøtz).

Treatment of the second group of eyes with 2 per cent pilocarpine nitrate solution was ineffective. Tension was not maintained below 30 mm. of mercury, or if it was lowered to between 20 and 30 mm. there was some loss of visual field after a trial period of treatment. In 2 of these eyes, 2 per cent epinephrine bitartrate solution was effective as an adjunct to pilocarpine; in 2 eyes it was partially effective, and in 2 eyes it resulted in a rise in tension. Operations which were not entirely successful had been done on 11 eyes. Carbaminoylcholine chloride (1.5 per cent) in 0.03 per cent zephiran solution maintained

the tension in all cases below 25 mm. of mercury (Schiøtz), and there was no further loss of visual field over periods up to twenty months. Six patients who had complained of morning headaches and aching in the eyes were relieved of these symptoms. *Intra diem* tension curves for these patients were established by averaging the tension as recorded on different visits to the clinic. Chart 4 shows the average *intra diem* tension curve of the eyes when receiving pilocarpine nitrate and of the same eyes when receiving carbaminoylcholine chloride.

The reduction of intraocular tension with carbaminoylcholine chloride was not always dependent on miosis. In 3 eyes after an iris inclusion operation in which the sphincter of the iris was cut the tension remained above 33 mm. of mercury (Schiøtz) postoperatively and 2 per cent pilocarpine nitrate solution was ineffective. However, tension was main-

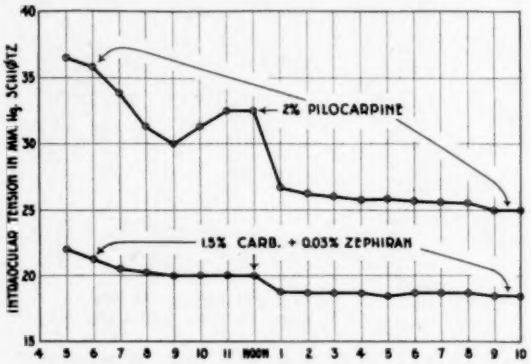

Chart 4.—The average *intra diem* tension curves of 34 eyes under treatment with carbaminoylcholine chloride–zephiran solution and with pilocarpine nitrate solution; the average of 1,482 tonometric determinations.

tained below 20 mm. by carbaminoylcholine chloride–zephiran solution instilled two or three times daily, and there has been no loss of field.

Systemic reactions to carbaminoylcholine chloride were carefully noted, since it is known to have profound effects on the autonomic nervous system when administered parenterally.[16] In 12 patients with hypertension (systolic, over 175; diastolic, over 90), the administration of the drug over periods of months did not alter the blood pressure. Many of the patients had advanced arteriosclerosis, but ill effects which could possibly be attributed to the drug were noted in only 1 patient. This patient collapsed twelve minutes after one of several instillations but recovered shortly. During the period of collapse there was a marked drop in the blood pressure. However, there was a history of similar attacks when she had not been receiving medication. Gastrointestinal

16. Starr, I.: Am. J. M. Sc. **193**:393, 1937.

symptoms due to increased peristalsis were expected in some patients, but none were observed.

Evidences of local irritation from the carbaminoylcholine chloride–zephiran solution were rare, since it is only slightly hypotonic and the p_H (7.05 to 7.21) borders on neutrality. During the first few days of treatment there was usually slight hyperemia of the conjunctiva, probably the result of vasodilatation rather than of local irritation. After several days little conjunctival hyperemia followed instillation of the drug.

Aching in the eye and headache usually were noted after the initial administration of the carbaminoylcholine chloride–zephiran solution but were uncommon after the third day of treatment. These symptoms were probably due to intense constriction of the iris sphincter and to stimulation of accommodation.

Gradle [17] has reported that a local sensitivity to carbaminoylcholine chloride develops after prolonged treatment, but Velhagen said that lack of sensitivity is one of the advantages of the drug. Only 1 case of local sensitivity was observed. After the first instillation of the drug there were considerable hyperemia and edema of the conjunctiva associated with evidences of irritation of the skin of the lids. No corneal involvement occurred, and the reaction subsided completely within twenty-four hours. Eosinophils were not found in scrapings of the conjunctiva. Synechias such as those noted after prolonged use of physostigmine were not evident.

Further studies will be required to determine definitely whether carbaminoylcholine chloride loses its efficiency after prolonged use, as does pilocarpine. In a few cases it has been possible to reduce the dose after months of treatment.

Studies on the combined use of carbaminoylcholine chloride and epinephrine bitartrate were inconclusive. In eyes without advanced changes in the anterior segment, epinephrine bitartrate administered once or twice weekly was found to serve as an adjunct to carbaminoylcholine chloride. In cases of advanced involvement the results were variable. One patient with extremely shallow anterior chambers and peripheral synechias was of particular interest. When epinephrine bitartrate was used as an adjunct to carbaminoylcholine chloride a rise in tension occurred in the right eye and a drop in tension in the left eye (chart 5).

Carbaminoylcholine chloride, like other miotics, has the disadvantage of requiring the patient with glaucoma to maintain a regular schedule of administration. In 4 patients the tension was controlled

17. Gradle, H. S.: Post-Graduate Course in Ophthalmology, George Washington University, Washington, D. C., 1940, vol. 6.

when carbaminoylcholine chloride–zephiran solution was administered at the hospital, but home treatment was unsuccessful. However, lack of regular medication was found to be less a factor with carbaminoylcholine chloride than with pilocarpine. The former drug in zephiran solution has a more prolonged action than pilocarpine; hence the tension is less apt to rise if one or two instillations are missed.

Carbaminoylcholine chloride was not effective in controlling the tension in 4 patients with advanced chronic noncongestive glaucoma. One of these patients, who had only one eye, had a small cornea (horizontal diameter, 10 mm.) and an extremely shallow anterior chamber. In the second patient swelling of the lens occurred one year after a successful trephine operation and was considered to be the cause of the elevated tension. There was no explanation for failure in the other 2 patients. In one of these, after an emotional upset bilateral acute glaucoma

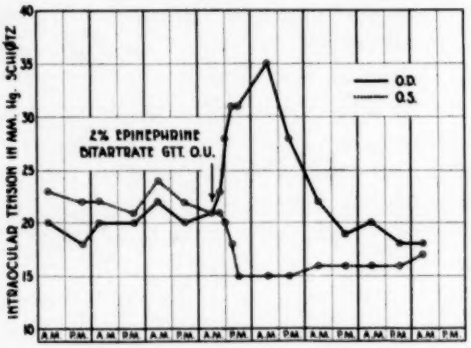

Chart 5.—The unpredictable effect of epinephrine bitartrate in cases of glaucoma simplex treated with carbaminoylcholine chloride.

developed which did not respond to the administration of physostigmine and sorbitol or to dehydration. An emergency operation was required. This patient was receiving carbaminoylcholine chloride at the time of the attack, and the tension had been effectively controlled during the preceding six weeks.

SUMMARY AND CONCLUSIONS

1. The normal cornea is relatively impermeable to carbaminoylcholine chloride in aqueous solution, but the drug is well absorbed when dissolved in a vehicle containing a surface tension–reducing agent, e. g. zephiran. Massage of the cornea through the lids further enhances absorption.

2. When precautions are taken to insure its absorption the drug reduces intraocular tension, is a powerful miotic and produces spasm

of accommodation. In 1.5 per cent solution its action is not only more pronounced than that of 2 per cent pilocarpine nitrate solution but more prolonged.

3. In many cases of advanced glaucoma simplex the drug in zephiran solution controls the tension and prevents further loss of visual field after pilocarpine has failed or even after failure of pilocarpine following unsuccessful operation. In cases of early involvement the drug controls the tension more effectively than pilocarpine and may be administered less frequently.

4. Carbaminoylcholine chloride in zephiran solution is stable and nonirritating, and no ill effects are noted from prolonged administration. Systemic reactions and local sensitivity to the drug are rare.

PIGMENTARY DEGENERATION OF THE RETINA

ROLE OF THE MELANOPHORE HORMONE OF THE PITUITARY GLAND IN PIGMENTARY DEGENERATION OF THE RETINA

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AND
FRANCIS HEED ADLER, M.D.
PHILADELPHIA

There are few ocular conditions that have aroused as much speculation and about which knowledge is still so meager as retinitis pigmentosa. It is generally accepted that the term retinitis is poorly applied and that the pathologic process is essentially a degenerative one. The term tapetoretinal degeneration is therefore much more appropriate. However, familiarity with the original term and common usage will doubtless maintain retinitis pigmentosa as a descriptive diagnosis, at least in ophthalmic literature.

The etiology of this condition has for many years aroused considerable controversy. The theories which have been advanced are (1) that the disease is primarily a degeneration of the neuroepithelium and (2) that it is caused by vascular sclerosis in the choroid. The consensus [1] now is that the primary disturbance is in the neuroepithelium and that the choroidal and glial sclerosis is secondary. The pathogenesis of the neuroepithelial degeneration, however, is still to be settled. The most acceptable postulates are (1) that the degeneration is caused by a hereditary abiotrophic defect and (2) that it is caused by an endocrine dysfunction. One must accept its hereditary nature,[2] but to do so should not deter attempts to unearth other factors that may play a part in this so far hopeless affliction.

From the Department of Ophthalmology, University of Pennsylvania School of Medicine.

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Read at the Seventy-Seventh Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 30, 1941.

1. (*a*) Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1940, vol. 3, p. 2779. (*b*) Verhoeff, F. H.: Microscopic Observations in a Case of Retinitis Pigmentosa, Arch. Ophth. **5**:392 (March) 1931.

2. Nettleship, E.: On Retinitis Pigmentosa and Allied Diseases, Roy. London Ophth. Hosp. Rep. **17**:1, 1907-1908. Marmor, J., and Lambert, R. K.: Laurence-Moon Biedl Syndrome: Its Relation to the General Problem of Retinitis Pigmentosa, Arch. Int. Med. **61**:522 (April) 1938.

Investigators who propose the theory that retinitis pigmentosa is caused by an endocrine dysfunction advance the following arguments to support their thesis: (1) that retinitis pigmentosa is frequently found in association with the Laurence-Moon-Biedl syndrome; (2) that there is a close embryologic relationship between the optic vesicles and the diencephalon, and (3) that the melanophore hormone, secreted by the pars intermedia of the pituitary gland, may affect the pigment layer of the retina.

The present study is concerned with the last of these postulates. The general problem of the etiology of retinitis pigmentosa has not recently been reviewed, and many of the conclusions and suppositions that have been presented in the literature have been based on inference rather than on direct experimental approach. It is fully realized, however, that there are many aspects to this problem, that there are several factors to be considered and that they cannot all be subjected to a direct investigative study. The investigative work reported here is an attempt to correlate and clarify one aspect of the problem.

RETINITIS PIGMENTOSA AS A MANIFESTATION OF AN ENDOCRINE DYSFUNCTION

The association of retinitis pigmentosa with pituitary dysfunction was first suggested in a study of cases of the Laurence-Moon-Biedl syndrome (obesity, polydactylia, hypogenitalism and mental retardation). This syndrome has been considered by many authorities to be caused by pituitary dysfunction because of its close resemblance to other so-called pituitary syndromes—e. g. dystrophia adiposogenitalis, first described by Fröhlich,[3] in 1901. Laurence and Moon [4] reported the syndrome in 1886, but it was not until 1922 that Biedl [5] drew attention to the familial nature of the affliction. The literature on this syndrome has recently been reviewed by Cockayne and co-workers.[6] There seems to be little doubt that the patients frequently exhibit some evidence of endocrine dysfunction. The available postmortem studies have not shown any characteristic lesion.[6]

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3. Fröhlich, A.: Ein Fall von Tumor der Hypophysis cerebri ohne Akromegalie, Wien. klin. Rundschau **15**:883 and 906, 1901.

4. Laurence, J. Z., and Moon, R. C.: Four Cases of "Retinitis Pigmentosa" Occurring in the Same Family, and Accompanied by General Imperfections of Development, Ophth. Rev. **2**:32, 1866.

5. Biedl, A.: Geschwisterpaar mit adiposo-genitaler Dystrophie, Deutsche med. Wchnschr. **48**:1630, 1922.

6. Cockayne, E. A.; Krestin, D., and Sorsby, A.: Obesity, Hypogenitalism, Mental Retardation, Polydactyly, and Retinal Pigmentation, Quart. J. Med. **4**: 93, 1935. Sorsby, A.; Avery, H., and Cockayne, E. A.: Obesity, Hypogenitalism, Mental Retardation, Polydactyly, and Retinal Pigmentation, ibid. **8**:51, 1939.

Because of the association of skeletal defects, such as polydactylia of mesodermal origin, and other defects, such as changes in the retinal pigment, which is epiblastic in origin, Cockayne and co-workers suggested "that the syndrome is determined by two recessive genes of the same chromosome or that it is dependent on some chromosome error such as a dislocation or translocation."

The laboratory studies carried out on patients with retinitis pigmentosa are suggestive but not in themselves diagnostic of pituitary dysfunction. Patients with retinitis pigmentosa have been shown by some investigators to have thyroid disturbances,[7] abnormalities in water and salt metabolism,[8] diminished dextrose tolerance,[9] hypogenitalism,[9b] and the presence of a melanophore-dispersing substance in the blood and urine.[10] Zondek,[7b] Viallefont,[11] Mamola and Bellina,[12] Pavía and Bidegain [13] and others have reported on the administration of pituitary preparations to patients with retinitis pigmentosa. Their reports, though not enthusiastic, have all claimed definite subjective improvement. This improvement in their opinion lends considerable support to the theory of an endocrine basis of the disorder.

ASSAY OF THE MELANOPHORE HORMONE

Early in the studies on the physiology of the pituitary gland it was realized that this gland has some effect on the pigment-bearing cells in cold-blooded animals. Hogben [14] in 1922 found that if the entire pituitary of the frog was removed the animal became pale and remained pale irrespective of its surroundings or state of adaptation. The skin melanophores were contracted at all times. If the gland was only

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7. (*a*) Nagayma, Y.: Ueber thyreotrope Substanzen im Harn bei Patienten von Degeneratio pigmentosa retinae, Acta Soc. ophth. japon. **40**:1239, 1936. (*b*) Zondek, H.: Diseases of the Endocrine Glands, Baltimore, William Wood & Company, 1935.

8. (*a*) Zondek.[7b] (*b*) Zondek, H., and Wolfsohn, G.: Retinitis pigmentosa und Hypophyse, Schweiz. med. Wchnschr. **70**:162, 1940.

9. (*a*) Zondek and Wolfsohn.[8b] (*b*) Dax, E. C.: Retinitis Pigmentosa, Quart. J. Med. **9**:263 (Oct.) 1940.

10. (*a*) Dax.[9b] (*b*) Dax, E. C.: A Melanosome Dispersing Substance in Blood and Urine in Cases of Retinitis Pigmentosa, Tr. Ophth. Soc. U. Kingdom **58**:227, 1938.

11. Viallefont, H.: Sur les rapports de l'hypophyse et de la rétine à propos de certaines rétinites pigmentaires, Ann. d'ocul. **173**:33, 1936.

12. Mamola, P., and Bellina, G.: Nuove vedute sulla patogenesi e sulla terapia della retinite pigmentosa, Rassegna ital. d'ottal. **4**:699, 1935.

13. Pavía, J. L., and Bidegain, M. O.: Hipófisis y retina, Cong. argent. de oftal. (1936) **2**:465, 1938; abstracted, Zentralbl. f. d. ges. Ophth. **42**:439, 1939.

14. Hogben, L. T., and Winton, F. R.: The Pigmentary Effector System: III. Color Response in Hypophysectomized Frogs, Proc. Roy. Soc., London, s.B **95**:15, 1923.

partially removed, i. e. the pars tuberalis was destroyed, the frog became dark and the skin melanophores were expanded and remained that way even if the animal was light adapted. The same condition of expanded melanophores can be obtained by the injection of preparations of the posterior lobe of the pituitary gland into the dorsal or the ventral lymph sac of the frog. The duration and the extent of the darkening depend on the concentration of the solution employed. In mammals the melanophore-dispersing hormone is formed by the pars intermedia of the pituitary gland (Zondek and Krohn [15]). The melanophore hormone free of other factors can readily be extracted from powdered posterior lobes (Stehle [16]).

Various procedures have been used in an attempt to obtain a satisfactory method of assaying preparations of the melanophore hormone. Whole frogs,[16] hypophysectomized frogs [17] and pieces of frogs' skin [18] have all been utilized in the attempt to establish a reliable method for determining the potency of the hormone. To date the most satisfactory test subject would appear to be the hypophysectomized frog (Teague [17]).

Krogh [19] and McLean,[20] using a perfusion method, were the first to attempt to determine the melanophore hormone content of blood. The hindlegs of a frog were perfused separately, the material to be assayed was perfused through one leg and the concentration that would cause minimal darkening of the skin was determined. This method proved fairly sensitive but was unsatisfactory when human serum was used because of the marked vasoconstriction that occurred. McLean determined that the hormone is carried entirely in the plasma. The perfusion of dextrose, urea, creatinine and uric acid of the same or of higher concentration as that found in human blood was without effect. Subsequent investigators, however, have injected the material to be tested into a lymph sac or into the peritoneum, thus obviating some of the difficulties and restrictions of the perfusion method. Dax [10b] has reported a melanophore-dispersing factor in the blood of patients with retinitis

15. Zondek, B., and Krohn, H.: Hormon des Zwischenlappens der Hypophyse (Intermedin): II. Intermedin im Organismus (Hypophyse, Gehirn), Klin. Wchnschr. **11**:849, 1932.

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19. Krogh, A.: The Pituitary Principle in Circulating Blood, J. Pharmacol. & Exper. Therap. **29**:177, 1926.

20. McLean, A. J.: The Anuran in Bio-Titration of Pituitrin, J. Pharmacol. & Exper. Therap. **33**:301, 1928.

pigmentosa. The blood was extracted with alcohol and the extract injected into the dorsal lymph sac of a normal frog. Jores [21] suspended small pieces of frogs' skin in human serum and noted the expansion of the melanophores under the microscope. There is a lack of uniformity in the various methods that have been tried.

PIGMENT MIGRATION IN THE RETINA AND ITS RELATION TO THE MELANOPHORE HORMONE

Angelucci,[22] Arey [23] and others have shown that when a frog is light adapted the retinal pigment is expanded and can be seen microscopically to extend between the rods and the cones as far as the external limiting membrane. If the animal is dark adapted the pigment granules are found to be closely packed about the cell nuclei outside the layer of rods and cones. The pigment migration is not caused by the extension and retraction of the cell processes but by the movement of the pigment granules in the cytoplasm of relatively fixed cells. The skin melanophores differ in this respect: Their cell processes extend and retract much like pseudopodia.

The striking control of the skin melanophores of the frog by pituitary activity would suggest that the relationship be reinvestigated with regard to retinal pigment migration. Jores [24] and Matuo [25] studied the effects of hypophysectomy and the injection of pituitary extracts on retinal pigment migration. Their reports were conflicting, and apparently neither controlled the temperature of the dark-adapted frogs. This is exceedingly important, as both Detwiler [26] and Arey [23] have shown that the position of the retinal pigment in the dark-adapted frog can be made to vary by temperature changes alone. Temperature is without effect, however, on the light-adapted animal.

Matuo [25] reported that hypophysectomy did not influence pigment migration in the retinas of either light-adapted or dark-adapted frogs. He stated, however, that the injection of pituitary hormone in normal

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21. Jores, A.: Untersuchungen über das Melanophorenhormon und seinen Nachweis im menschlichen Blut, Ztschr. f. d. ges. exper. Med. **87**:266, 1933.

22. Angelucci, A.: Histologische Untersuchungen über das retinale Pigmentepithel der Wirbelthiere, Arch. f. Physiol., 1878, p. 353.

23. Arey, L. B.: The Movements in the Visual Cells and Retinal Pigment of the Lower Vertebrates, J. Comp. Neurol. **26**:121, 1916.

24. Jores, A., and Caesar, K. G.: Ueber die Wirkung des melanophores Hormons auf Pigmentwanderung und Pupillenweite des Froschauges, Arch. f. d. ges. Physiol. **235**:724, 1934.

25. Matuo, K.: Ueber die Pigmentwanderung der Pigmentzellen der Froschnetzhaut, Okayama-Igakkai-Zasshi **47**:2387, 1935; abstracted, Zentralbl. f. d. ges. Ophth. **36**:497, 1936.

26. Detwiler, S. R., and Lewis, R. W.: Temperature and Retinal-Pigment Migration in the Eyes of the Frog, J. Comp. Neurol. **41**:153, 1926.

and in hypophysectomized frogs caused an expansion of pigment in the dark-adapted retina as well as an expansion of the skin melanophores, whereas this injection had no effect on the retinal pigment of light-adapted frogs. Dubois Poulsen [27] corroborated this finding but used normal frogs only. Jores [24] found that hypophysectomy per se did not influence pigment migration in the retina but that injection of a posterior pituitary extract caused a contraction of the pigment when the animal had been light adapted and no effect when the animal had been dark adapted. This is the reverse of Matuo's findings. Drouet and Florentin,[28] using normal frogs, found that the injection of intermedin, a pituitary extract, caused a maximal contraction of the pigment granules in dark-adapted frogs whereas in light-adapted animals the contraction of the granules was also pronounced. They expressed the opinion that this contraction of the granules from their normal expanded condition in light adaptation caused the photophobia they noticed in their frogs! All these investigators have stated the belief that the retinal pigment is influenced to some extent by the melanophore hormone of the pituitary gland, though they do not agree as to what the effect may be. Jores [24] said that even though the pituitary has been removed, the hypothalamus may secrete an appreciable amount of the hormone; so the characteristic light and dark position of the retinal pigment can still be seen in the hypophysectomized animal.

In describing subjective experiments Jores [24] claimed that the instillation of melanophore hormone into the conjunctival sac accelerated dark adaptation in human beings and lowered their final threshold. Basile [29] likewise stated that the hormone lowered the threshold in both normal persons and persons with retinitis pigmentosa. Buschke [30] was unable to confirm this, and Jeandelize and Thomas [31] found just the opposite effect, that the threshold was raised. The effect on the retinal pigment of pituitary extracts containing active melanophore hormone is, therefore, far from being settled, and we felt that the problem merited reinvestigation.

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27. Dubois Poulsen, A.: Effets de l'extrait hypophysaire et de l'adrénaline sur les franges de l'epithélium pigmentaire de la rétine de la grenouille, Compt. rend. Soc. de biol. **125**:248, 1937.

28. Drouet, P. L., and Florentin, P., cited by Jeandelize, P., and Drouet, P. L.: L'oeil et l'hyphophyse, Tr. Internat. Ophth. Cong. (1937) **3**:227, 1938.

29. Basile, G.: Sull' azione dell' ormone melanoforo in soggetti normali ed in soggetti affetti da retinite pigmentosa, Ann. di ottal. e clin. ocul. **67**:412, 1939.

30. Buschke, W.: Zur Frage der Einwirkung des Melanophorenhormons auf die Dunkel-Adaptation des menschlichen Auges, Klin. Wchnschr. **13**:1785, 1934.

31. Jeandelize, P., and Thomas: Influence de l'intermédine et de l'adrénaline sur les courbes d'adaptation dans quelques cas de rétinite pigmentaire, Bull. Soc. d'opht. de Paris **49**:608, 1937.

EXPERIMENTAL PRODUCTION OF PIGMENTARY CHANGES IN THE RETINA

Despite the great interest in pigmentary disturbances of the retina, there have been comparatively few experimental investigations of this phenomenon. Wagenmann [32] in 1890 described a change in the retina closely simulating pigmentary degeneration and following section of the posterior ciliary arteries and nerves. Nicholls,[33] however, has since shown that this is not the typical lesion of retinitis pigmentosa. Verhoeff [1b] in the pathologic examination of a human eye showed rather conclusively that the pathologic process is not primarily of a vascular nature.

Friedenwald and Chan [34] injected uveal pigment into the posterior chamber of rabbits' eyes and observed the subsequent reaction. They found considerable pigment scattered about the fundus, rather pronounced phagocytosis of the pigment cells and disorganization of the retinal structure. They expressed the opinion that the histologic changes could be accounted for on the hypothesis that the primary lesion is in the neuroepithelium and is followed by infiltration of the retina by melanin granules.

Kalt [35] was able to produce pigment changes in the retina of rabbits by the subcutaneous injection of 1 cc. per kilogram of 4 per cent sodium iodate solution every other day. Within ten days a scattering of pigment was visible in the retina. Histologically there were many clumplike aggregations of pigment, with partial destruction of the rods and cones. He concluded that the retinal picture closely resembled that of retinitis pigmentosa and that it might be caused by the cirrhotic changes in the liver, which were pronounced in all the animals given injections. Sato [36] produced pigment changes in kittens' retinas with daily intravenous injections of 0.1 to 0.4 cc. of epinephrine hydrochloride solution. After several weeks there was a diffuse disturbance of the retina. Histologically it consisted of a destruction of the neuroepithelial cells and swelling of the pigment cells, with dispersion and agglutination of

32. Wagenmann, A.: Experimentelle Untersuchungen über den Einfluss der Circulation in den Netzhaut und Aderhautgefässen auf die Ernährung des Auges, insbesondere der Retina, und über die Folgen der Sehnervendurchschneidung, Arch. f. Ophth. (pt. 4) **36**:1, 1890.

33. Nicholls, J. V. V.: The Effect of Section of the Posterior Ciliary Arteries in the Rabbit, Brit. J. Ophth. **22**:672, 1938.

34. Friedenwald, J. S., and Chan, E.: Pathogenesis of Retinitis Pigmentosa, Arch. Ophth. **8**:173 (Aug.) 1932.

35. Kalt, M. E.: Rétinite pigmentaire expérimentelle sur le lapin, Bull. Soc. d'opht. de Paris **49**:304, 1937.

36. Sato, T.: Die Einwirkung des intravenös eingespritzen Adrenalins auf den Augapfel, Acta Soc. ophth. japon. **41**:1009, 1937; abstracted, Zentralbl. f. d. ges. Ophth. **40**:638, 1937.

the pigment granules. The rods and cones were thinned, and their nuclei showed degenerative changes. There was marked gliosis, and pigment was found in the supporting fibers.

Thus far all attempts to produce pigment changes experimentally have been carried out on animals with fully developed retinas. Either the circulation has been interfered with or foreign or chemical materials have been injected into the animal. The suggestion advanced that the condition is an endocrine disturbance would naturally lead one to attempt confirmation with the experimental animal. Hyperfunction of the pars intermedia can be partially stimulated by the injection of active melanophore hormone. The young gray rat would appear to be the ideal experimental animal for this procedure, since the rat's retina is in the embryonic stage at birth and during the first ten days undergoes a rapid transition through the stages of inner and outer neuroblastic layers to the layers of the normal retina. The rat's retina is also made up mostly of rods, with relatively few cones, and the embryonic cells are more susceptible to biologic changes than the fully developed cells.

THE PROBLEM

In the present investigation an attempt was made to determine whether the melanophore hormone of the pituitary gland bears any relation to pigmentary changes in the retina. This was done in three types of experiments. The first series of experiments was planned as a means of determining the action of the melanophore hormone on the retinal pigment of normal and of hypophysectomized frogs. Secondly, by repeated injections of purified melanophore hormone into young rats an attempt was made to reproduce the retinal lesions seen in retinitis pigmentosa. Thirdly, an attempt was made to confirm Dax's [10b] finding of a melanophore-expanding substance in the blood of patients with retinitis pigmentosa.

EFFECT OF THE MELANOPHORE HORMONE ON RETINAL PIGMENT MIGRATION IN THE NORMAL AND IN THE HYPOPHYSECTOMIZED FROG

The following observations were conducted last winter; approximately 100 frogs (Rana pipiens) were used. The technic of removal of the pituitary gland was essentially that described by Hogben [37] and Teague.[38] After operation the frog was not used for experimental

37. Hogben, L. T.: A Method of Hypophysectomy in Adult Frogs and Toads, Quart. J. Exper. Physiol. **13**:177, 1922.

38. Teague, R. S.; Noojin, R. O., and Geiling, E. M. K.: The Hypophysectomized Frog (Rana Pipiens) as a Specific Test Object for Melanophore Hormone of the Pituitary Body, J. Pharmacol. & Exper. Therap. **65**:115, 1939.

purposes for a week to ten days. The color of the frog depends on the type of operation performed. If the pituitary gland is completely removed the frog becomes very pale; the web melanophores contract and remain contracted irrespective of their surroundings. If the gland is only partially removed, the pars tuberalis being destroyed, the animal becomes very dark, the melanophores are maximally expanded and the frog resembles the animal that has had an injection of melanophore hormone.

SERIES 1.—Normal, pale (complete removal of the pituitary) and dark (incomplete removal of the pituitary) frogs were light adapted at room temperature in a shallow white enamel pan for twenty-four hours. The light source was a 60 watt lamp 24 inches (61 cm.) above the pan. The animals were then decapitated and their eyes rapidly removed. The cornea was pierced with a knife needle to ensure rapid fixation. Held's solution [38a] was used as a fixative, and a modified technic suggested by Detwiler [39] was used for all the histologic studies. The sections were all taken to include a portion of the optic nerve in order to insure the obtaining of identical portions for examination. They were cut at 7 microns and were stained with Harris' hematoxylin and eosin.

SERIES 2.—This procedure was repeated with animals which had been dark adapted for twenty-four hours in a shallow enamel basin in a photographic dark room. The water in the pans was just deep enough to cover their bodies. The pans were placed in a sink and the running water adjusted to a temperature between 17 and 18 C. Frequent checks showed that the water in the pans was at the same temperature. The room temperature was controlled at about 20 C. The fixative was maintained at the temperature of the water for one-half hour before use. The eyes were enucleated under a photographic red lamp and allowed to remain in the fixative in the dark for one-half hour.

SERIES 3.—Normal and hypophysectomized frogs were used; one half of the frogs were light adapted and the other half dark adapted. In each lot one half of the frogs were given injections of 0.15 mg. of melanophore hormone prepared according to the method of Teague.[17] It had previously been determined that 0.001 mg. of this hormone would cause minimal darkening of the skin and expansion of the melanophores in a hypophysectomized frog. The solution, freshly prepared every twenty-one days, was kept in the dark and each lot assayed on at least 4 frogs. The frogs receiving 0.15 mg. of the hormone were very dark within one half hour. They were decapitated one hour after the injections and the eyes prepared in the usual manner. Before the hypophysectomized frogs were used their web melanophores were examined under the microscope to see that they were maximally contracted.

RESULTS

When the sections from the normal light-adapted frogs were examined the retinal pigment was always found to be maximally dispersed. The pigment granules could be seen extending up between

38a. Saturated solution of potassium dichromate, 4 parts; 10 per cent concentration of solution of formaldehyde U. S. P., 4 parts; glacial acetic acid, 1 part.

39. Detwiler, S. R.: Studies on the Retina, J. Comp. Neurol. **36**:125, 1923.

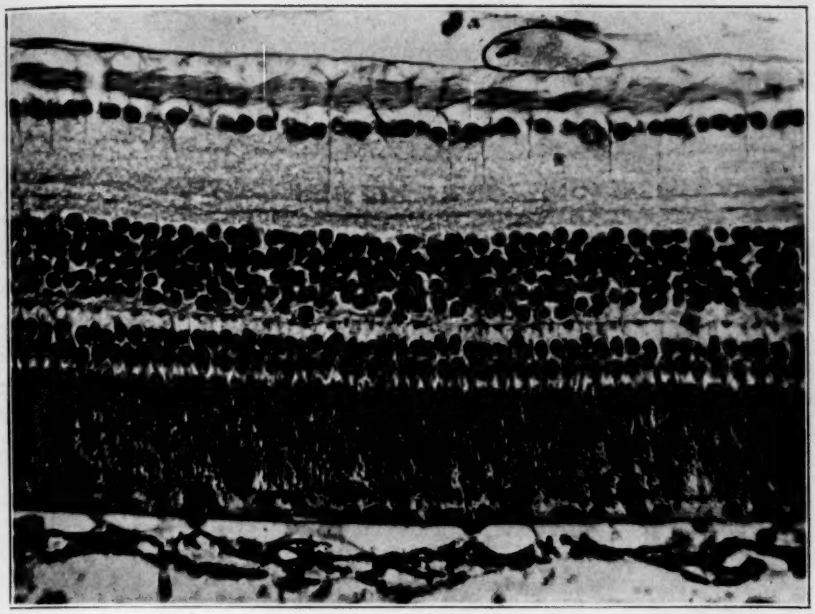

Fig. 1.—Section of a light-adapted retina, showing maximum expansion of the pigment granules. (Hematoxylin and eosin stain; × 320.)

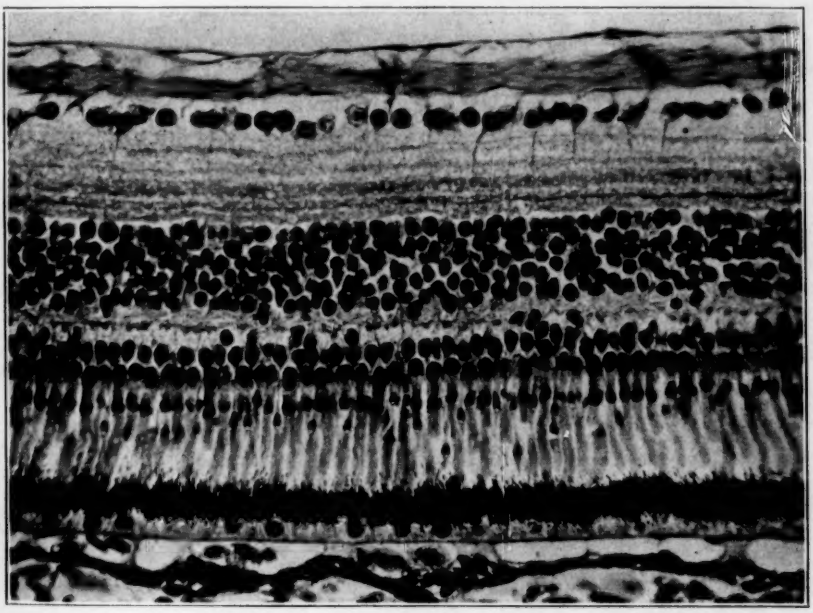

Fig. 2.—Section of a dark-adapted retina, showing maximum contraction of the pigment granules. Note the extension of the cone myoids. (Hematoxylin and eosin stain; × 320.)

the rods and the cones as far as the external limiting membrane (fig. 1). The pigment appeared to be evenly distributed, and contraction of the cone myoids was clearly demonstrated. In the dark-adapted frogs the pigment cells were massed in a thick layer outside the layer of rods and cones (fig. 2). The cone myoids could be seen to be expanded, as is characteristic of dark adaptation. The results were uniform, and none of the sections aroused any question as to whether the eye had been light or dark adapted. The injection of the melanophore hormone was without significant effect on the retinal pigment or on the cone myoids of the normal light-adapted or dark-adapted frog.

Complete hypophysectomy did not change the characteristic light or dark position of the retinal pigment. The histologic changes were the same as in normal frogs. The melanophore hormone was likewise without effect on the retinal pigment.

In the dark frogs, whose pituitaries had been only partially removed, the retinal pigment exhibited the usual changes. No abnormal histologic changes were seen.

EFFECT OF MELANOPHORE HORMONE ON THE RETINAL PIGMENT OF THE GRAY RAT (MUS NORVEGICUS)

Active melanophore hormone was prepared from dried posterior pituitary powder according to the method of Teague.[17] This was assayed on hypophysectomized frogs. Each cubic centimeter of the solution is calculated to contain 0.33 mg. per cubic centimeter. In all our assays it was found that 0.001 mg. would produce minimal darkening of the skin and expansion of the web melanophores. The solution was prepared fresh every two weeks and each lot assayed. Seven litters of gray Wistar rats (Mus norvegicus) were used. In the first two litters the mothers were given 1 cc. each of the stock solution on the two days preceding the birth of their offspring. The hormone was injected subcutaneously. The young were then given injections of 0.1 cc. subcutaneously every day, and the mother received 1 cc. The mortality was rather high after this procedure; the injections were apparently painless but the mothers did not look after the young, which is not uncommon when rats are subjected to experimental procedures during the nursing period.

In subsequent litters only the young were given injections, one half of them being kept as controls. After the first week they were given 0.5 cc. three times a week and after the first month 1 cc. three times a week. The eyes were removed at various intervals up to six months and were fixed and sectioned by the same method as the frogs' eyes.

In the 28 eyes examined the normal histologic picture prevailed. There was no difference in the distribution of retinal pigment in the normal animals and in the animals given injections.

ASSAY FOR AN ACTIVE MELANOPHORE-EXPANDING SUBSTANCE IN HUMAN BLOOD

In this investigation it was decided to use serum from whole blood rather than to extract the blood with chemical reagents before using it. Our procedure was to inject 1 cc. of serum into the dorsal lymph sac of a frog which had been light adapted for one hour in a shallow white enamel pan. The injection was made as far up on the back as possible to avoid leakage of the serum through the point of entrance of the needle.

In our first series we used normal frogs, the control frogs receiving at the same time 1 cc. of physiologic solution of sodium chloride or of normal serum. After the injection of the serum to be tested the frogs were watched for one to two hours. Maximal or submaximal darkening of the skin melanophores was considered a positive reaction.

Results of Assay for an Active Melanophore-Expanding Substance in Human Blood

Ocular Diagnosis	Total Number of Patients	Total Number of Tests	Number of Patients with Positive Reactions	Number of Tests on Patients with Positive Reactions	Number of Patients with Negative Reactions	Number of Tests on Patients with Negative Reactions
Normal frogs used						
Retinitis pigmentosa	43	57	12	16	31	41
Other conditions	10	14	4	6	6	8
Hypophysectomized frogs used						
Retinitis pigmentosa	12	17	1	2	11	15
Other conditions	20	35	1	2	19	33

With this method 71 tests were done on 53 patients, of whom 43 had retinitis pigmentosa and the remaining 10 other ocular diseases, such as myopia, choroiditis and Leber's disease. There were 16 positive reactions among 12 of the patients with retinitis pigmentosa and 4 positive reactions among the other patients, as shown in the accompanying table.

During the last few months, only hypophysectomized frogs were used for this test. Frogs operated on ten to twelve days previously were used throughout. The frogs were all pale, and their web melanophores were seen to be maximally contracted when observed under the low power microscope. The frogs were light adapted for one hour in the manner described, but the temperature of the water was maintained at 15 to 17 C. The frogs were never used more than twice. They were all examined one to two hours after the injection. A positive reaction was one in which there was noticeable darkening of the skin and microscopic evidence of expansion of the web melanophores.

In all, 52 tests were done on 32 patients, 12 of whom had a clinical diagnosis of retinitis pigmentosa (see accompanying table). Seventeen tests were done on these 12 patients, with only 1 positive reaction. Thirty-five tests were done on the other 20 patients; 1 patient, who had congenital syphilis and was receiving treatment, gave a positive reaction.

RESULTS

Using hypophysectomized frogs we obtained far fewer positive reactions than when we used normal frogs. Several patients who repeatedly had a positive reaction when normal frogs were used repeatedly had a negative reaction when hypophysectomized animals were used. The activity of serum kept in the refrigerator for twenty-four hours is neither enhanced nor destroyed. In our hands and with our procedure this test has not proved to be of any value in the diagnosis of retinitis pigmentosa.

COMMENT

Our experiments would indicate that the melanophore hormone bears no relation to retinal pigment migration in the frog. The retinal pigment is epiblastic in origin and apparently differs in its reactions from the skin melanophores. The conflicting reports of other investigators on the relation of the melanophore hormone to pigment migration might possibly be ascribed to lack of proper temperature control. With adequate temperature control the exposure to light would appear to be the most important factor controlling retinal pigment migration in the frog.[40] In mammals the reaction of the retinal pigment to light is absent (Arey[41]).

The injection of melanophore hormone into young gray rats over a period of several months is apparently without effect on the pigment layer of the retina. If retinitis pigmentosa is caused by hyperfunction of the pars intermedia one might expect some changes in the pigment epithelium of the retina, particularly because the hormone was administered when the retina was in the embryonic stage. Moehlig and Pino[42] suggested that the lesion in the retina is caused by hypofunction of the pars intermedia; the pigment in the retina would thus not be bound by the hormone and might be scattered about the fundus. Jeandelize and Drouet[43] also stated that retinitis pigmentosa may be caused by

40. McDonald, P. R.: Unpublished data.

41. Arey, L. B., in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 2, p. 780.

42. Moehlig, R. C., and Pino, R. H.: Retinitis Pigmentosa, Arch. Ophth. **23**:1257 (June) 1940.

43. Jeandelize, P., and Drouet, P. L.: Troubles endocrines et plus spécialement hypophysaires dans les hémorragies récidivantes du corps vitré, Bull. Soc. d'opht. de Paris **48**:260, 1936.

hypopituitarism. We have not noted any retinal changes in frogs which were hypophysectomized four to five weeks before their eyes were removed for study. The effect of hypofunction of the pituitary will, however, require further investigation.

The various tests that have been used for detection of an active melanophore-expanding substance in blood and urine have not, in our opinion, been conclusive. The lack of uniformity in an accepted test, the relative infrequency of its application as compared with that of other rather universally accepted tests for pituitary hormones—i. e. the pressor and oxytoxic factors—would indicate that either the melanophore-expanding hormone is difficult to detect or that the method of assay is at fault. The method of Krogh [19] and McLean [20] has been mentioned. Jores,[21] who used Trendelenberg's [18] technic of suspending isolated pieces of skin in blood serum, stated that that method was satisfactory. We tried this method but did not find it reliable. Colin and Drouet [44] and Jeandelize and Drouet [43] have reported finding a melanophore-expanding factor in the urine in patients with hyperthyroidism, migraine or recurrent vitreous hemorrhages and in those with known pituitary disease. Dax [10b] and Ridell [45] have found a melanophore-expanding substance in the blood and urine in patients with retinitis pigmentosa. These investigators all used normal frogs. Shen [46] has shown that the normal frog will respond by darkening to many drugs as well as to the melanophore hormone. Teague [38] has reinvestigated this whole problem; his conclusions are that hypophysectomized frogs do not react by darkening to the drugs that will affect a normal frog, that the hypophysectomized frog is a specific test subject for the melanophore hormone and that the hypophysectomized frog is more sensitive to the hormone than the normal frog. Our results indicate that testing for the melanophore-expanding factor in serum in hypophysectomized frogs seldom gives a positive reaction.

The work of Hogben and Slome [47] and Steggerda and Soderwall [48] suggests that the pars tuberalis secretes an "anti-melanophore-expanding"

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44. Colin, R., and Drouet, P. L.: Présence dans l'urine de certaines malades d'un principe mélonaphoro-dilateur, Bull. Acad. de méd., Paris **109**:794, 1933.

45. Ridell, W. J. B.: Multiple Factors in Hereditary Eye Disease, Tr. Ophth. Soc. U. Kingdom **49**:275, 1939.

46. Shen, T. C. R.: The Mechanism of the Melanophore Expanding Action of Several Drugs and Its Relationship to the Internal Secretion of the Hypophysis in Frogs, Arch. internat. de pharmacodyn. et de thérap. **62**:295, 1939.

47. Hogben, L. T., and Slome, D.: The Pigmentary Effector System: VIII. The Dual Receptive Mechanism of the Amphibian Background Response, Proc. Roy. Soc., London, s.B **120**:158, 1936.

48. Steggerda, F. R., and Soderwall, A. L.: Relationship of the Pars Tuberalis to Melanophore Response in Amphibia (Rana pipiens), J. Cell. & Comp. Physiol. **13**:31, 1939.

hormone. If the pars tuberalis alone is destroyed, the skin melanophores are maximally expanded and remain that way. This naturally suggests that the pars tuberalis controls pigment contraction. Thus the melanophore response may be caused by the presence of an excess of the melanophore-expanding hormone or inhibition of the melanophore-contracting hormone. The lack of uniformity in the results of tests for an active melanophore-expanding principle in human blood may be due in part to the presence or absence of this "antihormone." Unpublished observations of Dr. J. Q. Griffith, in which the melanophore reaction of human beings became positive after irradiation of the pituitary region, lend some support to this hypothesis.

CONCLUSIONS

That retinitis pigmentosa is caused by pituitary dysfunction is suggested by certain clinical and embryologic relationships. Scanty evidence based on an experimental approach has hitherto been presented to bear out this conclusion. We have attempted to investigate these relationships from an experimental biologic standpoint. Our results indicate that:

1. The injection of purified melanophore hormone has no effect on retinal pigment migration in the frog.

2. The injection of melanophore hormone has no effect on the retinal pigment of the rat.

3. Hypophysectomy, complete or incomplete, has no effect on retinal pigment migration in the frog.

4. The assay for an active melanophore-expanding substance in the blood of patients with retinitis pigmentosa is not of significant diagnostic value.

Dr. J. Q. Griffith, of the Robinette Foundation, provided criticism and suggestions. Dr. E. J. Farris, of the Wistar Institute of Anatomy, supplied gray Wistar rats and made available the facilities of the institute. The histologic sections were prepared by Mr. T. Maxwell, B.A., B.S., in the Department of Histology, University of Pennsylvania School of Medicine.

SUPERFICIAL PUNCTATE PARENCHYMATOUS KERATITIS

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Superficial punctate parenchymatous keratitis may be defined as a disturbance of the subepithelial tissues of the cornea resulting in the formation of minute flecks and wavy lines. It occurs with conjunctivitis. It is usually bilateral and disappears without leaving any trace. There is no involvement of the corneal epithelium.

The symptoms of the disease are set down from the records of 195 cases observed during thirteen years. They are as follows:

Recurrent attacks of mild or severe conjunctivitis occur in association with photophobia, lacrimation and redness, particularly of the bulbar conjunctiva. These symptoms may be severe or mild, or they may be chronic with acute exacerbations. The feeling of a foreign body is often the most marked symptom. The patient may be awakened in the night by discomfort; the following morning the eye is moderately red and he goes to his physician to have the supposed foreign body removed. In some cases chronic redness of the eye is the only symptom and the ophthalmologist is consulted because of the appearance. During acute exacerbations there may be edema of the upper lid causing a slight or marked narrowing of the palpebral fissure. In some cases this may last for a long time, with or without moderate redness of the eye. Such edema and drooping of the lid may present difficulties in diagnosis, being mistaken for ptosis due to an organic cause. The condition appears to be due to tonic spasm of the orbicularis oculi muscle.

There is rarely chemosis, and if present it is slight. There may be slight ciliary congestion, which is likely to be masked by the more marked conjunctival congestion. The conjunctiva, however, is usually not brilliantly red; the congestion often is chronic or passive except during the exacerbations of the disease, when it is violently acute, the eye immediately becoming very irritated and red, with profuse weeping, marked edema of the lids, blurring of the vision and considerable pain. The pain consists of the sensation of "cutting" or of the presence of sand or a very sharp foreign body in the eye. The patient often insists that a foreign body is present. There are extreme photophobia and

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blepharospasm; the pupil is moderately contracted, showing irritation of the iris. On examination no foreign body is found. The irritation is relieved in a few moments with phenacaine (holocain) and epinephrine, which agents seem to act as a specific. If the cornea is then *deeply* stained with fluorescein it will be found to be thickly dotted with typical minute flecks of an iridescent green. Associated with the flecks may be seen wavy "glass lines;" both are subepithelial. In some cases the flecks are arranged in chains somewhat like chains of cocci. The wavy lines were described in Vogt's [1] single case of "glass lines." They look like the wavy lines which appear on the surface of smooth water or in a defective pane of glass.

The patient in whom this disease was first discovered was a woman aged 40 in good health and of a favorable financial and social status. She had suffered from redness of the left eye for twenty years and had had acute exacerbations during which the eye was fiery red and there were irritation and lacrimation. Hers was the worst and most persistent case seen. Careful search with the slit lamp after many sittings showed a few very minute white flecks in the cornea. They were too minute to be seen except with the slit lamp. They consisted of fine white angular points in the superficial layers of the cornea and did not involve the epithelium. I wish to emphasize the noninvolvement of the corneal epithelium. The flecks were of a peculiar alabaster whiteness, not round but angular. They could not be resolved by high magnification into component gray spots but appeared to be homogeneous. They seemed to disappear after an acute exacerbation and to reappear rapidly during a subsequent attack. On disappearing they left no trace, and the cornea remained perfectly clear. In some cases a few flecks remained between the exacerbations, and in such cases the eye usually was chronically red. The flecks take a fluorescein stain brilliantly; after staining they have a scintillating iridescence that has not been observed in any other corneal lesion. Examined with the slit lamp with high power and a very narrow slit, the flecks are seen to be in the most superficial layers of the cornea. In no case has there been observed a disturbance of the corneal epithelium.

In the case noted there were but three or four of the typical lesions in the intervals but during the exacerbations there were many. The whole cornea was thickly studded with them, and the eye was fairly red, with profuse lacrimation, marked feeling of a foreign body, slight ciliary congestion, conjunctival congestion and edema of the upper lid. The last-named symptom simulated a slight ptosis and could easily have been mistaken for it, since the eye except during acute attacks was

1. Vogt, A.: Lehrbuch und Atlas der Spaltlampenmikroscopie des lebenden Auges, ed. ?, Berlin, Julius Springer, 1930, pp. 264-265.

normal in appearance. The condition in this case, after having existed for twenty years, was promptly cured by local treatment with phenacaine and epinephrine and by the use of the Shahan thermophore applied to the cornea. The patient has been observed for twelve years without a subsequent attack.

In 1932 I [2] reported 11 cases of this corneal disturbance before the American Academy of Ophthalmology and Otolaryngology. Since that time there have been encountered and studied 195 cases. A further report is deemed of value, since more information has been gathered concerning this frequent condition. Some of the less frequently observed symptoms noted since the first report are as follows:

Fatigue of the eyes on near work, associated with headaches and blurring of vision. The blurring is due, I believe, to increased secretion of mucus.

Burning and itching during the exacerbations and to a lesser degree during the intervals, suggesting an allergic reaction.

Photophobia without other ascertainable cause.

Chronic redness of the eye without other symptoms. This has been observed in a number of cases.

Moderate chemosis, often boggy and confined to the bulbar conjunctiva over the lower portion of the globe.

Halos about lights. This, I believe, is due to an increase in the secretion of mucus, which spreads over the cornea.

Facial tic. This was observed in 6 cases. They were carefully studied and all causes eliminated except those involving the eye. The tic was bilateral in 4 cases.

Tenderness of the globe. This was noted in a few cases and aching of the eye not associated with tenderness in a few.

Tonic blepharospasm. In 2 cases this was severe. The patients had been almost totally incapacitated by inability to keep the eyes open. Exhaustive studies did not reveal the cause of the marked contraction of the orbicularis. The flecks in association with the wavy lines in the corneas was pronounced in these cases. The patients were suffering from lack of exercise, fresh air and sunshine, since they could not go out alone. As a result there was some malnutrition and anemia. Local treatment and correction of the abnormal way of living resulted in cure of the corneal condition and relief of the blepharospasm.

Chronic headache. In a few cases this was the chief complaint. It was associated with redness of the eyes and asthenopia, which had persisted for some years. The headache was aggravated by use of the eyes for near work.

2. Davis, W. T.: Superficial Parenchymatous Punctate Keratitis, Tr. Am. Acad. Ophth. **37**:115, 1932.

Bilateral puffiness of the lower lid associated with redness of the eyes and slight ptosis. This condition, present in several cases, created a most unwholesome appearance, making the patient appear very dissipated.

Epiphora and chemosis. One unusual case is worth citing. Dr. E. D., aged 66, in excellent health, had suffered from epiphora for several years. The puncta and canaliculi had been slit and the lacrimal ducts probed. Various collyriums and preparations of silver nitrate applied to the palpebral conjunctivas had not helped him. There was an unusual edema of the bulbar conjunctiva confined to the lower half of the globe of each eye. This was not associated with irritation or redness and was of long standing. The only symptoms were the chemosis and epiphora. A few typical flecks were found in each cornea. The epiphora and chemosis were relieved after two weeks of the usual treatment.

So far as I am aware, there has been no previous description of superficial punctate parenchymatous keratitis (S. P. P. K.) as a clinical entity. After writing my original report, in going over Vogt's [1] atlas I noted one mention of this condition. Vogt did not refer to it as a clinical entity.

The possibility of its being a corneal manifestation of disturbance of tissue common to many causes must be considered. In the majority of cases, however, it appears to be a clinical entity as far as the symptoms and treatment are concerned. The lines referred to are described by Vogt as glass lines. These may be the prominent lesion in some cases. The flecks, however, are always present and usually predominate.

The cause of "conjunctivitis" of this type, characterized particularly by chronic redness of the eye, will not be recognized unless the cornea is studied with the slit lamp. Undoubtedly many chronically irritated and red eyes are treated for the various forms of conjunctivitis when the real cause is S. P. P. K. or a similar corneal lesion. The cause of the drooping of the lid is not altogether clear. It is not always associated with edema and may be due to a moderate tonic spasm of the orbicularis oculi muscle.

DIAGNOSIS

Staining of the cornea and use of the slit lamp will promptly show the lesion as described. It has undoubtedly been diagnosed and treated as conjunctivitis and thus aggravated and prolonged. There can be no reason for confusing S. P. P. K. with superficial punctate keratitis (S. P. K.); the latter can be diagnosed with the loupe and the lesions are in the epithelium. The subjective symptoms in the acute cases are similar to those of neuropathic keratitis, but the corneal flecks stain an iridescent green with fluorescein, and this leaves no doubt as to the diagnosis of S. P. P. K. The subjective symptoms in some cases are similar to those of diplobacillus conjunctivitis.

Is this form of corneal disturbance a clinical entity? Personal communications from English ophthalmologists who have seen similar cases in India and China and from French ophthalmologists who have observed such cases in Africa and Indo-China cause me to feel rather certain that they have not observed the disease herein described. Kirkpatrick,[3] Duke-Elder,[3] T. Harrison Butler [3] and others during the past decade have been inclined to look on S. P. K. as a clinical entity. With regard to S. P. P. K. Duke-Elder [3] said:

> There are a lot of conditions like this in the literature, and many that one sees from day to day. Some of them look like an inflammatory condition, but more of them look like corneal dystrophy. My own impression is that most of them are dystrophic in nature and associated with vague vitamin and endocrine imbalances. It seems to me that you have got enough of a single type to warrant calling it a clinical entity, and I should certainly publish it as such if I were you.

In the same communication he said that similar forms of keratitis occur in India and Egypt, suggesting a dietary cause.

In the cases of endothelial dystrophy followed by epithelial disturbances during the course of the disease discussed by Duke-Elder, none of the patients showed epithelial disturbances at the beginning. The epithelial dystrophy of Fuchs [4] may be ruled out; a gross lesion, this may be observed with the unaided eye and is a disturbance of the epithelium. Objection has been made to the statements that the deeper structures of the cornea will stain with fluorescein through the intact epithelium and that if the lesions of S. P. P. K. stain there must be an involvement of the corneal epithelium.

Duke-Elder [5] noted that Fromm and Groenouw demonstrated in 1891 that if fluorescein solution was allowed to remain in the conjunctival sac for a few minutes behind closed lids instead of being immediately washed out it penetrated the intact epithelium. Von Hippel,[6] who widely employed this method, in 1902 showed that the deep parenchyma became colored if the epithelium was damaged. This deep staining by fluorescein is equally valuable as a means of determining the depth of interstitial lesions or the extent of endothelial defects. This is mentioned at this writing since there appears to be a wide difference of opinion as to whether fluorescein will penetrate the intact corneal epithelium. It

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3. Personal communication to the author.

4. Fuchs, E.: Keratitis Punctata Superficialis, in Text-Book of Ophthalmology, translated by A. Duane, ed. 8, Philadelphia, J. B. Lippincott Company, 1924, p. 563.

5. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 2005.

6. von Hippel, E., cited by Duke-Elder.[5]

would appear that one is correct in assuming that the lesions of S. P. P. K., which are subepithelial, may be stained through the intact epithelium.

Kirkpatrick [3] said:

> The condition you describe is similar to that in the epidemic I observed in Madras, India, from 1918 onward. The slides represent an almost precisely similar lesion. During Wright's time, however, the disease appeared to assume a more virulent character and associated cyclitis was more frequently observed. I think he was of the opinion that it was of the nature of a virus disease, but I myself was unable to form any positive opinion regarding the cause.

T. Harrison Butler [3] recently said:

> One must be careful in scheduling a new disease of the cornea. Of this I am well aware, and this paper has been written with the hope that others will investigate the condition to deny or confirm my observations. Vogt has described many kinds of epithelial conditions, dystrophies if you like, and I have figured some in my book, and I am wondering if some of these are separate clinical entities. What you describe is, I am sure, something new, and, as is always the case, once a condition is discovered the number of instances grows rapidly for a time.

The last sentence reflects what has been in my mind; hence I avoided writing further on the subject until more cases were accumulated. The number having reached 195 in a period of thirteen years, I am beginning to believe that the condition is a clinical entity. It has not been observed as an epidemic. The description by Kirkpatrick,[3] Wright [3] and others does not tally with my observations in S. P. P. K. Except in rare cases S. P. P. K. is bilateral; in most cases one eye is more severely involved than the other. No change in the sensitivity of the cornea and no complicating uveitis have been noted.

Davidson [7] said that Otchapovsky, in attempting to classify the keratitides, introduced a group of true keratoconjunctivitides. Davidson stated that a virus was being increasingly designated the cause of corneal diseases. Vazquez-Barriere [8] included in his etiologic classification of the keratitides a group due to a virus, including in it keratitis superficialis punctata, the metaherpetic keratitis of Vogt and relapsing erosions. Duke-Elder [5] classified a number of keratitides in a group called keratitis superficialis punctata, which he did not consider a disease entity. The S. P. P. K. described by me may possibly come under this heading.

It would seem that knowledge does not yet make possible a classification of the keratitides; yet there are new forms being recognized and reporting of them should be encouraged in order that more may be

7. Davidson, M.: Occupational Keratitides and Corneal Dystrophies, Arch. Ophth. **21**:673-683 (April) 1939.

8. Cited by Davidson.[7]

known about them and some day an understanding of the subject be achieved. The diagnosis of subacute or chronic conjunctivitis should be made only after careful study of the cornea.

Davidson said that occupational S. P. K. is not a serious condition. He emphasized the fact, however, that the diagnosis of subacute or chronic conjunctivitis should not be made without careful examination of the cornea. Vogt [8] described the symptoms of the epithelial keratitides in general as photophobia and blurring of the vision. Other investigators,[8] reporting on occupational S. P. K., mentioned halos about lights, burning and lacrimation. These are among the symptoms I have ascribed to S. P. P. K. Thiel [8] described the lesions of S. P. K. as minute gray discrete lesions in and beneath the epithelium. These lesions superficially resemble those I have described in S. P. P. K., but I have observed no involvement of the epithelium and the lesions are not gray but alabaster white.

Samoilov [8] and Gifford [8] also described forms of S. P. K. of occupational origin. These forms, however, appear to be entirely epithelial. There appears to be no occupational factor in S. P. P. K. as described in this paper, since the patients were from all walks of life. One has less opportunity to study workers of the artisan class in Washington, D. C., since there are no factories in the city. The etiologic studies have been unsatisfactory because the patients were from so many walks of life, were of all ages and represented the two sexes about equally.

It is possible that the disease is of nutritional origin. It would be extremely difficult to prove or disprove that it is. It is true that the eating habits of the nation have changed greatly in the last decade, with metabolic alterations resulting. Nutritional factors may be operative in a certain number of cases. Mass handling of vegetables, cooking them on electric stoves and keeping them warm in steam tables destroys more or less the vital principles. They are little else than cellulose when they reach the table. Food is old when it reaches hotels and restaurants and still older when it reaches the consumer. Citrus fruits are picked so green that the chemical process of ripening is never set in motion. Thus, many such fruits contain little or no sugar and probably no vitamins or other fresh principles. Milk is some time in reaching the consumer and is pasteurized; hence there is a reduction of its fresh principles. Such examples may be multiplied many times. The net result in my opinion is that a great part of the nation is suffering from nutritional disorder, whether it is called avitaminosis or by another name. I believe that many corneal lesions have a food deficiency basis, not because of lack of food but because of its handling and preparation.

Of the 195 patients observed, 53 were male; the youngest was 11 years old and the oldest 89. The majority were clerks, school children

or professional men. Their activities were diverse, but they were of the so-called white collar class. Age and occupation do not seem to be factors. The majority of the patients, however, were between 20 and 50 years of age.

Excessive use of tobacco, coffee, tea or in some cases alcohol may lead to nutritional disturbances. Lack of sunshine and outdoor exercise may be other factors.

Wright [9] said that Fuchs may not have observed many of the severe forms of keratitis such as one sees in epidemics. If the initial stages are mild, it is possible, he said, to miss this disease (S. P. K.) or keratitis disciformis et uveitis anterior unless it progresses to a late residual form. What Wright said may possibly apply to S. P. P. K., yet I have watched this disease for thirteen years and have observed no indication of epithelial involvement early or late, no scarring of the cornea and no disciform keratitis. It is possible that under certain conditions S. P. P. K. might assume epidemic form, with the complications and sequelae mentioned by Wright in his description of S. P. K. What he described cannot be the form of keratitis which I have described, since in his disease the epithelium is prominently and early involved. There is no diffuse haziness of the cornea, involvement of the endothelium or uveitis in S. P. P. K.

When I visited Madras the first time, in 1906, en route to the United States after serving with the Army in China and in the Philippines, I made notes on the conjunctivitis which appeared there in epidemic form and was often accompanied by punctate involvement of the cornea. My stay in India was limited, and facilities for study were lacking at that time. I am inclined to think that what I saw then was the S. P. K. described by Wright.

Wright [9] gave a table of corneal diseases which he thought might at some stages present symptoms analogous to those of S. P. K. It is possible that the disease I have described may be a phase or stage of one or of many diseases or lesions of the cornea. I am yet to be convinced of this.

Wille [10] described a keratitis noted in Java which in no way resembles S. P. P. K. The symptoms are suggestive, however. He described a number of cases in which there was severe blepharospasm which was cured when the keratitis was cured.

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9. Wright, R. E.: Superficial Punctate Keratitis, in Report of the Government Ophthalmic Hospital, Madras, India, 1931.

10. Wille, W. A.: Keratitis Ramificata Superficialis and Its Connection with Asthenopia, Brit. J. Ophth. **22**:705-722 (Dec.) 1938.

Kirwan [11] described an epidemic of punctate keratitis in Bengal, India, in 1934. His description seems to tally with Wright's and with Kirkpatrick's. He mentioned involvement of the epithelium, which at once distinguishes the condition from S. P. P. K.

Recently I saw a patient with bilateral severe superficial keratitis; a huge number of flecks involved the cornea. They did not stain with fluorescein. The epithelium was roughened. The condition resulted after the patient, having petted a prize bull which was at the time being groomed for a cattle show, rubbed his eyes. It resembled S. P. P. K. and cleared up in a few days with palliative treatment.

Zur Nedden [12] described an epidemic of S. P. K. which occurred in Germany in 1938-1939. In many cases the condition followed a superficial injury to the cornea, and in many instances it occurred without injury. The conjunctivitis was the primary lesion; there were chemosis, edema of the eyelid and frequently swelling of the preauricular lymphatic gland and of the cheek. These, zur Nedden said, are prominent diagnostic signs. The lesions of the cornea occurred later in the deeper layers, with involvement of the epithelium. The eye remained white, but the cornea did not become clear for many months. The sensibility of the cornea was reduced. It does not appear that this tallies with the description of S. P. P. K.

I should like to state that bacterial studies of the conjunctival secretions in my series of cases, including inoculations of rabbits' corneas, have all given negative results.

Schneider,[13] in a short report on disease of the anterior part of the bulb of unknown cause, said that this disease attacks the conjunctiva and begins with photophobia, lacrimation, sensation of a foreign body, hyperemia and edema of the palpebral margin and of the bulbar conjunctiva. The usual symptoms of ocular irritation were marked. The corneal lesions were different in extent, form and color. In some cases the lesion appeared in the form of a single comparatively large spot, whereas in others it was distributed all over the cornea in fine dots conglomerated into fine stripes or spread profusely in small cloudy vesicles. Diffuse corneal opacity due to the agglomeration of the vesicles in the epithelium was sometimes observed. Occasionally plastic iritis was observed. It is obvious that this disease is entirely different from S. P. P. K.

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11. Kirwan, E. W. O.: Epidemic Superficial Punctate Keratitis in Bengal, Folia ophth. orient. **1**:345-357, 1934.

12. zur Nedden: Ueber Keratitis superficialis punctata, Klin. Monatsbl. f. Augenh. **102**:487-490, 1939.

13. Schneider, R.: Kurzer Bericht über eine Erkrankung des vorderen Bulbus-Abschnittes unbekannter Ursache, Klin. Monatsbl. f. Augenh. **102**:130, 1939.

Smitmans [14] described similar diseases in Germany. His patients complained of nasopharyngeal catarrh and symptoms resembling those of grip, with fever, malaise and headache preceding the ocular involvement. The lesions were mostly epithelial, with gray, superficial frosting of the cornea giving the appearance of ground glass. I have seen several such cases in this country, and they bear no relation to the disease under discussion.

Feigenbaum,[15] in a paper on S. P. K. in Palestine, described a form in which the epithelium of the cornea was markedly involved. The condition in the cases in India reported by Wright did not seem to tally with this disease.

Dr. Sanford R. Gifford, Dr. Arnold Knapp and others made suggestions for the study of this condition.

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ABSTRACT OF DISCUSSION

Dr. Sanford R. Gifford, Chicago: Dr. Davis has given ophthalmologists something to think about in his report of 195 cases which suggest to him an entity described as superficial punctate parenchymatous keratitis. Two questions in particular seem to be suggested by his report: First, does his description really indicate that the epithelium is entirely spared by the process, or is the epithelium, according to the standards which guide most ophthalmologists, to some extent involved? Second, what relation if any does the condition he describes bear to what is ordinarily called superficial punctate keratitis, to the condition recently described by a number of Germans as keratoconjunctivitis epidemica and to Dimmer's keratitis nummularis? Also, how many patients with a similar condition are being seen by other ophthalmologists, and how is their condition being classified?

In answer to the first question, it would seem that most ophthalmologists would be inclined to accept staining with fluorescein as evidence that the corneal epithelium is in some way involved. There need not be an actual defect in the epithelium, but I believe there must be some damage to the epithelial cells if they absorb and retain the stain as it is usually applied. Small infiltrates will not raise or erode the corneal surface appreciably but will often damage the epithelium sufficiently so that the stain will be absorbed and retained in the damaged areas.

In answer to the second question, a study of reports on large series of cases, such as that of Wright on the Madras epidemic, seems to indicate that there are all stages between typical superficial punctate keratitis as described by Fuchs and the condition described by Dr. Davis.

Wright (*Brit. J. Ophth.* **14:** 257, 1930) observed 923 cases in 1928 and 1929 and found that the lesions varied from small areas visible only

14. Smitmans, F. K.: Aussprache über die Keratoconjunctivitis epidemica 1938. Einführender Vortrag, Med. Klin. **35:**235-236, 1939.

15. Feigenbaum, A.: Note sur la kératite ponctuée superficielle épidémique en Palestine, Rev. internat. du trachome **16:**18-21, 1939.

with the slit lamp, through infiltrates of the usual Fuchs type to much larger ones like those of disciform keratitis. Some of the lesions did not stain, while others did, and this was considered evidence of involvement of the corneal epithelium. There were also lesions of the marginal punctate type. Hamilton (*Brit. J. Ophth.* **25:** 1, 1941) reported 92 cases observed in Tasmania, Australia, during nine years; the picture was exceedingly varied. The same is true of the German cases reported within the past four years. The condition was especially frequent in the Rhineland and in Munich. Zur Nedden (*Klin. Monatsbl. f. Augenh.* **102:** 487, 1939) observed 200 cases within a year in Düsseldorf and Schneider (*Klin. Monatsbl. f. Augenh.* **102:** 130, 1939) 150 in Munich. Senger saw the condition in 200 cases in a few months during 1939. Becker (*Klin. Monatsbl. f. Augenh.* **102:** 866, 1939), Löhlein, Grüter, Gilbert and others have reported on similar cases and agreed in most respects in describing the clinical picture. Emphasis was placed by most of the German authors on the existence of a fairly severe conjunctivitis which as a rule preceded the corneal lesions, and on the fact that the corneal lesions were often so small that they could be seen only with the slit lamp. The condition was called keratoconjunctivitis epidemica because of the great number of cases occurring at certain times, although evidence of direct contagion was seldom present. Hobson (*Am. J. Ophth.* **21:** 1118, 1938) reported on 16 cases in which there were fine gray dots in the second layer of the cornea apparently resembling those described by Dr. Davis. He called the condition epidemic superficial punctate keratitis.

In going over my own records I found that 17 cases had been listed during the past five years as instances of superficial punctate keratitis. I am certain that the condition has been seen in at least an equal number in clinics and in private practice but has escaped proper classification in the diagnosis file. In only 3 of the 17 cases was it of the typical Fuchs type, with infiltrates large enough to be seen grossly. The diagnosis in the others I put down in my own index as the "microform of superficial punctate keratitis." The condition seems to have been almost exactly like that described by Dr. Davis in his previous and in his present report and also, to my way of thinking, like that in some of the German cases. Conjunctivitis was marked in all but 5 of the cases and in a number had been treated as acute catarrhal conjunctivitis for some days before a slit lamp examination revealed its true nature. Unlike the German observers, however, I have never seen the condition in a stage when no corneal lesions could be observed with the slit lamp. All possible variations in arrangement of the lesions were seen. A nurse at Cook County Hospital had the most severe involvement. One eye was affected first and showed literally thousands of punctate and linear lesions. The cornea resembled a field which has been scraped thoroughly by a harrow in both directions. The condition was refractory to treatment but healed after about three months, with almost imperceptible scarring. Two years later the second eye was similarly affected, but healing was complete in three weeks. In half of the cases both eyes were involved. The number of lesions varied greatly, but ten to twenty-five could usually be counted, with others appearing as the original ones healed. The duration of symptoms varied from a week to several months.

Treatment was not very satisfactory. Cowan's 2 per cent potassium iodide solution with 2 drops of compound solution of iodine to the ounce (30 cc.) seemed to be of value in preventing fresh lesions while the original ones healed. When one eye was involved a dressing gave relief and seemed to promote healing. I have avoided applications of strong antiseptics to the lids, although Hamilton stated that the duration of symptoms was much shortened by a few applications of a preparation of silver. In the few cases in which the lesions were large these were touched with trichloroacetic acid as they appeared, and this seemed to promote rapid disappearance of individual infiltrates. In the more common microform such applications are neither possible nor advisable. In a few cases of severe involvement, such as that of the nurse mentioned, two or three doses of unfiltered roentgen radiation of not more than 80 roentgens each were employed and seemed to be of value, as is the case in dendritic keratitis. I have not used the packs of Pregl's iodine solution described by Cowan or the thermophore.

There seems to be good evidence that superficial punctate keratitis of the Fuchs type and also the keratoconjunctivitis epidemica described by German observers are due to infection with a filtrable virus. Ordinary bacteriologic investigation has as a rule given negative results. An exception was reported by Meesman and Bachmann (*Klin. Monatsbl. f. Augenh.* **105:** 1, 1940), who observed a diphtheroid bacillus, often associated with staphylococci. The organism resembled Bacillus xerosis, and it seems likely that it was a saprophyte. As evidence of a virus infection must be considered the usual absence of pathogenic bacteria and a few positive results from inoculation. Wright obtained positive results from 5 of 11 inoculations on the human cornea. Jancke (*Klin. Monatsbl. f. Augenh.* **105:** 7, 1940) made numerous inoculations in scarifications of the rabbit's cornea and in a subconjunctival pouch. By both these methods a number of positive reactions were obtained, the lesions resembling those of herpes. Jancke expressed the belief that a virus is responsible for the disease but that it is not identical with the herpes virus. Jess (*Klin. Monatsbl. f. Augenh.* **105:** 388, 1940) obtained positive results from 5 of 12 inoculations of the chorioallantoic membrane of the chick, the changes being those considered characteristic of a virus infection. Schneider failed to obtain positive results by the same method. A few inoculations on the rabbit's cornea made in the laboratory of Northwestern University Medical School gave negative results. The scarcity of active material in the corneal lesions probably accounts for many negative results, but it may be remembered that Jancke obtained positive results not only with material from corneal lesions but with scrapings of the inflamed conjunctiva.

Whether the keratitis nummularis described by Dimmer is a variety of superficial punctate keratitis and whether it is allied to the condition described by Dr. Davis seems difficult to decide. Its name designates round, or coin-shaped, lesions; in the original cases these were beneath the epithelium. Ješe (*Klin. Monatsbl. f. Augenh.* **96:** 219, 1936), who described 44 cases observed in Slovenia, Yugoslavia, during four years, stated the belief that it was a type of herpes. Aust (*Arch. f. Ophth.*

129: 576, 1933), however, who observed 27 cases in Vienna, expressed the opinion that it was a fungous infection and not a form of herpes. During the time these cases were observed I have seen the disease in only 2 cases in which it would be considered typical, but the conditions in some of Wright's cases seem to have resembled it.

Owing to the difficulties of checking one written description with another and to the fact that exact reproductions of the lesions through photographs or drawings have seldom been attempted, it seems impossible to differentiate the condition described by Dr. Davis from that in some of Wright's cases, in some of those said by the Germans to be instances of keratoconjunctivitis epidemica and in those which I have called cases of the microform of superficial punctate keratitis. Dr. Davis has done ophthalmologists a service in emphasizing the frequency with which the condition occurs and the importance of making a slit lamp examination in every unusual case of conjunctivitis, even when the cornea appears grossly normal.

Dr. Trygve Gundersen, Boston: It disturbs me a great deal to think that I have never seen a patient with superficial punctate parenchymatous keratitis. At least I have never seen one whose condition would fulfil the description given by Dr. Davis. I may be interpreting similar observations differently. Dr. Davis is certainly the first to describe this syndrome.

The diagnosis of superficial punctate parenchymatous keratitis depends entirely on the slit lamp observation of brightly stained flecks and wavy lines in the subepithelial layers of the cornea. Emphasis is placed on the bright staining of the flecks together with the normal appearance of the corneal epithelium. Oscar Wilkinson in his discussion of Dr. Davis' paper on the same subject in 1932 raised the question as to how this staining can occur when the epithelium is normal. I should like to raise this question again.

If one admits that the normal epithelium does not stain or allow fluorescein to pass through, one must ask Dr. Davis to relocalize the depth of these white lesions in the cornea. If they actually are in the epithelium and not at Bowman's level or beneath it, they conform precisely with those of Vogt's keratitis epithelialis disseminata. Keratitis epithelialis disseminata is a good descriptive term for a common corneal change occurring in a variety of conditions and is in no sense a disease entity. In my opinion keratitis epithelialis disseminata should be included in the differential diagnosis, since it really fits the description of superficial punctate parenchymatous keratitis more closely than does either superficial punctate keratitis or Fuchs's epithelial dystrophy.

For treatment Dr. Davis recommends the use of epinephrine and phenacaine. Therapeutic benefit from epinephrine solution dropped in the eye has never been clearly established. Phenacaine is much less innocent. With cocaine and the other members of its group of drugs it is a protoplasmic poison, and it is my firm conviction that its indiscriminate use in the eye, particularly in the presence of infection, should be condemned. It would be interesting to observe the results of treatment if these drugs were not used.

DR. WILLIAM THORNWALL DAVIS, Washington, D. C.: Dr. Gifford feels that the epithelium is involved. Careful study of the cases has shown no such involvement.

The condition described by the Germans as keratoconjunctivitis always involved the corneal epithelium, as does keratitis nummularis. I must emphasize this statement: In S. P. P. K. there is no involvement of the corneal epithelium that can be discovered by means of study now available. It is difficult to understand that for the corneal tissues to be stained the epithelium must be involved. I again refer to Duke-Elder's statement on this point. I am unaware of any basis for the accepted and prevalent belief that disturbance of the epithelium is necessary before the *cornea* will stain. I believe it to be true that the *epithelium* must be damaged before this layer itself will stain.

A careful perusal of the reports of Wright, Hamilton, zur Nedden, Senger and other authors mentioned by Dr. Gifford reveals that they all spoke of involvement of the epithelium at some stage of the disease they described. In no case of S. P. P. K. that I have observed has the epithelium been involved so that it was apparent with the high power of the slit lamp or with any other means of study. Some years ago I saw a nurse at the Washington Sanitarium and Hospital whose condition would fit closely the description of that seen by Dr. Gifford in the Cook County Hospital. It resisted all means of treatment for months. It bore no resemblance to S. P. P. K. and the recurrent attacks left scarring of the cornea. This patient was seen by de Schweinitz, Wilmer and Wheeler and by Wright, Elliott and Kirkpatrick, of England. No diagnosis was made.

Regarding Dr. Gundersen's discussion, may I invite his attention to the statement in my paper that the flecks discovered in my first case were *not* stained? Staining causes them to be quickly and easily seen. I fear I cannot admit that fluorescein cannot pass through the normal corneal epithelium. The location of the flecks appears to be beneath the corneal epithelium. When the cornea is stained, this becomes more apparent. This location is difficult or impossible to prove except by securing a specimen of the involved cornea for section and study. Obviously this is difficult, and so far it has been impossible.

In the 195 cases reported there was never evidence of disturbance of the epithelium with the use of phenacaine and epinephrine. Like de Schweinitz, I believe that the former has a curative value when properly used. I agree with Dr. Gundersen that the indiscriminate use of cocaine and kindred drugs and of epinephrine is improper. Cocaine destroys the superficial epithelial layer of the cornea, and its use except in surgical procedures is inadvisable. With the use of phenacaine and epinephrine the relief to the patient is immediate and the cure of the disease, if such it is, is prompt. In no case has there been a complication or involvement of the epithelium. In some cases there have been recurrences of the flecks after some days or weeks. This is unusual after treatment. In most of the cases there was a history of recurrence over long periods, sometimes for years, before treatment was instituted.

I am of the opinion that the thermaphore is the curative agent and probably acts by changing or stimulating the metabolism of the corneal tissues. If S. P. P. K. is due to a virus, it is entirely possible that it is

inhibited at the same time that the metabolism of the cornea is stimulated, with resultant prompt relief of the patient. In the earlier cases I used other methods and means without success.

It would be most gratifying if my two colleagues would note any cases of the condition I have tried to describe. Their observations would be of great value in proving or disproving the correctness of my observations.

May I express my thanks to these gentlemen for their full and frank discussion? It will be most helpful in further observations I have in mind. I trust that I may be able, after their discussions, to obtain a specimen of tissue for study and to pursue the study of the permeability or nonpermeability of the normal corneal epithelium to solutions of fluorescein.

ACTINOMYCES

RECOVERY OF THE STREPTOTHRIX IN A CASE OF SUPERFICIAL PUNCTATE KERATITIS

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Streptothrix has frequently been found in the canaliculus (Morax[1] and others), but its occurrence in other parts of the conjunctival sac has less commonly been observed. When present it usually produces granulomatous nodules on the bulbar conjunctiva (de Walsche,[2] Denti[3] and Liégard[4]) or on the retrotarsal folds (Bakly[5]). In the latter situation the resemblance of the lesions to trachomatous follicles has been noted by Morax[6] and by Knapp and Dwyer.[7] In Sicardi's[8] case the fungus was found in the scratch made by the stem of a plant. When nodules are not formed, varying types of conjunctivitis are produced. Dombray and Gault[9] reported a unilateral inflammation of the subacute

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4. Liégard: Ulcération mycosique de la conjonctive, Bull. Soc. d'opht. de Paris, 1925, pp. 153-155.

5. Bakly: Three Cases of Streptothrix Infection of the Conjunctiva, Tr. Ophth. Soc. U. Kingdom **41**:521-525, 1921.

6. Morax, V.: Conjonctivite chronique à Streptothrix Foersteri durant depuis un an et simulant le trachome, Bull. Soc. d'opht. de Paris, 1925, pp. 273-275.

7. Knapp, A., and Dwyer, J. G.: Acute Streptothrix Infection of the Conjunctiva, Arch. Ophth. **47**:497-499 (Sept.) 1918.

8. Sicardi, J. A.; Regules, U., and Talice, R. V.: Un cas intéressant d'actinomycose conjonctivo-sclérale d'origine traumatique, Ann. de parasitol. **14**:171-176 (March 1) 1936.

9. Dombray, and Gault, A.: Conjonctivite chronique due à une nouvelle espèce d'actinomyces, Bull. Soc. d'opht. de Paris, June 1938, pp. 409-412.

catarrhal type. The infections described by di Fede [10] and de Logu [11] were also unilateral but were largely confined to the angles and were characterized by abundant mucoid secretion. Membrane formation was reported by May [12] and a violently acute conjunctivitis by Knapp and Dwyer.[7] Corneal involvement usually takes the form of a raised nodule on the epithelial surface (Thies [13] and Davids [14]).

REPORT OF CASE

A 50 year old pipe fitter was first seen on April 25, 1940. He complained of watering of the left eye and the constant sensation of a foreign body in the same eye and stated that these symptoms had lasted for over a year. He had consulted many physicians and used many drops without relief. General physical examination, including roentgenograms of the teeth and sinuses, had revealed nothing abnormal, and the Kline blood test had been negative. Ophthalmologic examination showed that the vision in each eye was 20/40. With the exception of a few posterior cortical lenticular opacities the right eye was normal. The left eye revealed some slight velvety palpebral conjunctivitis. There were no follicles, and the puncta were normal and not congested. Scattered over the center of the cornea were several discrete staining areas. Several similar areas which did not stain were visible at about the level of Bowman's membrane, and a few opacities were seen to be elevated and covered by intact but thin epithelium. Sensibility was somewhat diminished. The interior showed cataractous changes similar to those in the right eye.

Smears and scrapings were taken from the conjunctiva but not from the cornea, and on the basis of the preliminary bacteriologic report the patient was given 10 drops of a saturated solution of potassium iodide three times a day by mouth and the following prescription was supplied to be used as eye drops:

Potassium iodide	0.30 cc.
Compound solution of iodine.....	0.12 cc.
Distilled water to make.....	30.00 cc.

Three days later the eye was much more comfortable, but the elevated nonstaining areas noted at the first examination had become denuded of epithelium and the former sites of the ulcers were marked by dim opacities. The administration of potassium iodide by mouth was discontinued, but the local treatment was carried on as before.

A week later the eye was white and comfortable, there was no staining, the vision was unchanged and there were several opacities in front of and behind Bowman's membrane.

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10. di Fede, N.: Un caso raro di congiuntivite actinomicotica (Studio clinico-sperimentale), Gazz. d. osp. **54**:868-871 (July 9) 1933.

11. de Logu, A.: Sopra un caso non commune di congiuntivite da actinomices, Boll. d'ocul. **9**:236-251 (March) 1930.

12. May, C. H.: Case of Streptothrix Involving the Conjunctiva of the Left Eye, Arch. Ophth. **46**:171 (March) 1917.

13. Thies, O.: Aktinomykose des Sehorgans, Klin. Monatsbl. f. Augenh. **86**: 55-58 (Jan.) 1931.

14. Davids, H.: Ueber Aktinomykose der Hornhaut, Klin. Monatsbl. f. Augenh. **67**:69-72 (July) 1921.

Two weeks later the patient complained of itching of the lids. A typical sensitivity reaction was encountered in the left upper and lower lids. The cornea was unchanged. Local treatment was stopped, and the dermatitis disappeared in a few days.

A month later the eye was white and the opacities unchanged. The patient failed to return for further examination.

BACTERIOLOGIC REPORT

Gram staining of direct films from the left conjunctiva revealed a moderate number of polymorphonuclear cells, a few short gram-positive filaments with granules and an occasional gram-positive diplococcus.

A culture of material taken from the left conjunctiva with a cotton swab moistened in 1 per cent dextrose infusion broth was rubbed directly over the

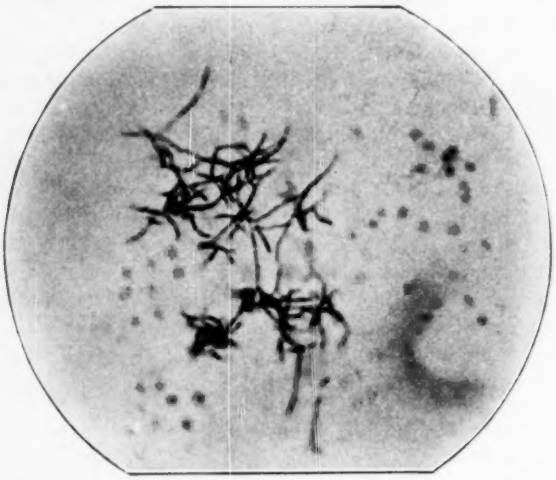

Fig. 1.—Streptothrix from conjunctival sac (× 1,000).

surface of a rabbit blood plate. A second swab was used for inoculation of chopped meat broth to which 2 cc. of ascitic fluid had been added. Similar cultures of material taken from the left lid were made.

On the original blood plate, after forty-eight hours' incubation at 37 C. under aerobic conditions, a small gray colony appeared, measuring 2 mm. in diameter. On further incubation for four days, seven grayish opaque round colonies were seen. These gradually changed to striated stellate colonies, measuring about 8 mm. in diameter.

Morphologic Aspect.—The isolated filament was gram-positive, showed granules and was nonacid-fast and nonmotile. It was long, uniformly thin and branched. The organism was transferred weekly to Difco's dehydrated Sabouraud dextrose agar, and it dissociated in a year. One colony showed dark gray pigment in the center and brown edges; the second dissociant had a dark yellow center with white edges.

Biochemical Activities.—The organism formed acid in dextrose but did not produce acid or gas in mannitol, maltose, saccharose, lactose or salicin. The methyl red reaction was negative. There was no production of indole, acetylmethyl

carbinol or hydrogen sulphide, but nitrates were reduced to nitrites. Litmus milk was unchanged. Loeffler's medium and gelatin were not liquefied.

Other Organisms Isolated.—The culture of material from the left lid showed colonies of Staphylococcus albus (hemolytic) and a few diphtheroid organisms. Mannitol and coagulase reactions were negative. Similar reactions were encountered in the cultures of material from the lid of the right eye.

A week later further material for culture was taken from each eye. From the conjunctiva of the left eye two colonies of Staph. albus and a few diphtheroid organisms were obtained. Mannitol and coagulase reactions were negative. Similar reactions were encountered in the cultures of material from the right conjunctiva and from the lids of each eye.

Six days later the cultures were repeated, and the observations were the same as at the preceding examination.

EXPERIMENTAL DATA

1. *Corneal Inoculation of a Rabbit.*—The living filament was suspended in a small amount of physiologic solution of sodium chloride, and with a 27 gage needle

Fig. 2.—Cornea of rabbit after inoculation with Streptothrix.

0.03 cc. of the suspension was injected into the cornea of a rabbit's eye. Two days later there was moderate swelling of the lids, with some conjunctivitis and discharge. An area of corneal infiltration 1 mm. in diameter was seen at the site of inoculation. The iris was hyperemic, but there was no hypopyon. At the next observation, made two days later, there was some purulent discharge and the swelling of the lids was so marked that they could not be separated and the cornea could not be seen. Not until four days after this had the swelling diminished enough to permit examination of the globe. On this occasion there was an abscess of the center of the cornea 3 mm. in diameter. The surrounding infiltration was well defined, but there was no vascularization and no hypopyon. Two days later the reaction was much diminished and the corneal lesion had become 1 mm. smaller, and thereafter healing was uneventful.

2. *Inoculation of Mice.*—An emulsified culture of the filament was made, and 0.5 cc. and 1 cc. were injected intraperitoneally into mice. No pathologic effects were observed.

3. *Inoculation of Guinea Pigs.*—Of the emulsified filament in broth 5 cc. was injected intraperitoneally and 0.2 cc. intradermally into guinea pigs. A small nodule formed at the site of the intradermal injection in seventy-two hours.

COMMENT

A branching filament, culturally and morphologically resembling the actinomyces group, was isolated from the conjunctiva of a patient with punctate keratitis. The corneal lesions were deeper than the superficial areas sometimes accompanying conjunctivitis and seemed to be similar in all respects to those of typical superficial punctate keratitis. The role of the fungus in the production of the corneal lesion can only be conjectured. It is significant, however, that the eye in which the streptothrix was not found remained healthy and that recovery from the keratitis in the other eye coincided with the disappearance of the fungus from the conjunctival sac.

PURKYNĚ

A PIONEER IN OPHTHALMOSCOPY

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"To know the truth that we lack knowledge is in itself a higher knowledge."—Humboldt.[1]

The importance and the amount of scientific knowledge hidden in the older literature are generally not realized and can hardly be imagined.

In gathering material for a book on Purkyně about to be published, I was astonished to find many unknown facts, some of which seem to be unbelievable. I had not intended to publish this or any other paper regarding my findings before presenting all the data I have compiled. But, being convinced that one fact is of such interest as to warrant its immediate publication, I have decided to announce it forthwith.

THE ORIGIN OF OPHTHALMOSCOPY

From the available evidence it clearly appears that the interior and the background of the eye of both animals and man were first observed by John Evangelist Purkyně, who made enormous contributions to the sciences, including medicine, and who has thus far not been equaled in the field of ophthalmologic research.

This ingenious investigator (fig. 1) was born in the small but historic Bohemian town of Libochovice on Dec. 17, 1787 and died in Prague on July 28, 1869.[2] Although descended from a centuries-old Hussite sect,[3] he was brought up as a Catholic and entered a religious order, which he left before taking the vows.

His most important discoveries were made during the early part of the twenty-seven years he spent as professor of physiology in Breslau, Germany. In Breslau he succeeded in making physiology an independent science by separating it from anatomy, with which it had until then been

1. Motto to volume 20 of *Magazin für die gesammte Heilkunde* (*Rust's Magazin*), 1829.

2. The year in which these ARCHIVES were founded.

3. The Calixtines, who demanded the cup in the Eucharist and also a limitation of the exclusive rights of the clergy. They were followers of Georg Calixtus, who advocated the union of all denominations.

combined. There also he founded the first physiologic institute of the world.

In the English and in much of the German literature his name is incorrectly spelled (Purkinje), and consequently it has been mispronounced. He is totally unknown to even the cultured layman, and the average physician vaguely knows of him only through Purkyně's "phenomena," "fibers" or "cells." There is, however, hardly any organ in the human body which he did not investigate, and it is indeed difficult to understand how he could be practically forgotten after having accomplished what he did.

Fig. 1.—John Evangelist Purkyně (1787-1869) as he looked after his return to Prague from Breslau, where he spent twenty-seven years. Note the Slavic and essentially Czech features. Purkyně came from a healthy peasant stock and lived to reach the age of 82.

In selecting and classifying the material for my work, I was particularly attracted by the following passages, translated from the tribute Heidenhain [4] paid Purkyně on the hundredth anniversary of his birth:

Gentlemen: I had the honor to invite you to a general session of our society in order to speak a word in reverent memory of a man who was born one hundred years ago today, who for almost a generation belonged to our society as well as to the University of Breslau, a true pioneer in a scientific field then only to be

4. Heidenhain, R.: Allgemeine Sitzung der schlesischen Gesellschaft für vaterländische Kultur am 17 December 1887 zur Feier des hundertjährigen Geburtstages von Joh. Ev. Purkinje, Jahresb. d. schles. Gesellsch. f. vaterl. Kult. **65**:1-15, 1887.

created, and who nevertheless today, even here in this spot, is hardly known and rarely recalled—John Evangelist Purkyně, the real founder of microscopic anatomy in Germany and at the same time the first to elevate physiology to the rank of an independent natural science.[5] . . . If Germany today stands unquestionably in the foremost rank in the field of medicine,[6] it was Purkyně who laid the foundation thereof by his establishment of the teaching of experimental physiology.[7] . . . Two little volumes, "Beiträge zur Kenntnis des Sehens in subjectiver Hinsicht" ["Contributions to the Knowledge of Subjective Vision"] [8] reveal a world of hitherto unknown optical phenomena.[9] Modern research workers still enjoy these fruits of Purkyně investigations. They invariably find in them something new and striking.[10] . . . While those of Purkyně's papers which were discussed were given considerable attention, one of his treatises, indeed the most outstanding work in the field of sense organs, was almost totally ignored. In his inaugural thesis at Breslau,[11] taking the eye as an example, he showed the physician how an organ should be examined for its normal and abnormal functions. The information contained in that thesis embraces all parts of the eye from the cornea to the retina, but it is obvious that Purkyně was given more to stimulation of thought and to observation of details than to following up productively what he had thought out and noticed. Thus it has happened that a great number of most important facts described in his papers were forgotten, to be rediscovered by other persons after many decades.

External objects are seen when light rays coming from them are united to form a picture on the retina of the eye. An understanding of how this happens is possible only if the curvature of the anterior surface of the cornea and of both surfaces of the lens are well determined. Purkyně found the means to measure those curvatures. He noticed that the spheric surfaces reflect pictures of external objects and proposed to measure with the microscope the size of those little images in order to determine the degree of curvature of the reflecting surfaces.[12] The little reflected images of a candle flame are reproduced exactly in his paper, and yet they were forgotten until fourteen years later, when the Parisian oculist Sanson [13] rediscovered

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5. Heidenhain,[4] p. 1.

6. This statement was made in the year 1887 and was meant to apply to that period.

7. Heidenhain,[4] p. 5.

8. Purkinje, J. E.: Beiträge zur Kenntnis des Sehens in subjectiver Hinsicht, Prague, Vetterl, 1819, and J. G. Calve, 1819; republished under the title: Beobachtungen und Versuche zur Physiologie der Sinne. Erstes Bändchen. Beiträge zur Kenntnis des Sehens in subjectiver Hinsicht, Prague, J. G. Calve, 1823, vol. 1; Beobachtungen und Versuche zur Physiologie der Sinne. Zweites Bändchen. Neue Beiträge zur Kenntnis des Sehens in subjectiver Hinsicht, Berlin, G. Reimer, 1825, vol. 2.

9. Those phenomena are not known even at present. These and other works of Purkyně have been translated from the various languages in which they were written and will be published soon. All the studies on the eye will be available in a separate book.

10. Heidenhain,[4] p. 11.

11. Purkinje, J. E.: Commentatio de examine physiologico organi visus et systematis cutanei, Breslau, University Press, 1823.

12. The ophthalmometer is based on this principle.

13. Whom Helmholtz called "the English eye physician" (Helmholtz, H.: Vorträge und Reden, Brunswick, Friedrich Vieweg & Sohn, 1896, vol. 1, p. 275).

them. They were, after more than thirty years, the basis for Helmholtz' investigations into the light refraction of the eye.

What a sensation was caused when, in the fifties, Helmholtz discovered the eye mirror, on which all modern ophthalmology is based. This instrument serves chiefly to illuminate the interior of the observed eye, so that the eyeground, which ordinarily is dark, may become visible. Purkyně described for this purpose, in his treatise, almost exactly the procedure which thirty years later Helmholtz used. Nowhere in the literature have I found an allusion to Purkyně's discovery.[14]

Since Heidenhain spoke before a mixed, or semiscientific, audience, containing many laymen, he did not find it necessary to give exact references to or quotations from the literature.[15] In spite of his authority, it was impossible to accept his statements as scientific proof, which had to be submitted for this report. The search for the literature in question presented great obstacles, because Purkyně's publications are practically unobtainable.

I knew that Purkyně made his investigations on the eye between the years 1818 and 1825, and since Helmholtz presented his ophthalmoscope for the first time in 1850, the difference in time of thirty years to which Heidenhain alluded appeared to be a correct estimate. I wanted to see Purkyně's original papers, and I was fortunate in finding two of his rare and important publications [8] dealing with his studies on the eye. The translation of these books revealed nothing regarding the ophthalmoscope. Soon after I had read the books I was informed by a great authority on Purkyně that Heidenhain must have been mistaken. But another careful reading of Heidenhain's address convinced me that there was no mistake and prompted me to seek further proof. The only work of Purkyně which I had still to study was his Latin dissertation [11] dealing with the method of examination of the eye. This work was impossible for me to consult, as the only copy deposited in the Army Medical Library does not circulate and in all Europe there exist only two or three copies. However, through Prof. Edwin G. Boring [16] I obtained from his assistant, Dr. Alfred G. Holway,[17] the negative photostats of the book and thus was able to photograph all of its fifty-eight pages. There I found the necessary evidence of Purkyně's method of ophthalmoscopy, and I so informed the mentioned authority on Purkyně, who then agreed but found it strange that Helmholtz had said nothing about it. Because the book [11] contains many valuable observations, it has been

14. Heidenhain,[4] pp. 12-13.

15. It was found that Heidenhain did quote the exact references in his excellent biographic sketch of Purkyně published the following year in the Allgemeine deutsche Biographie, Leipzig, von Duncker & Humboldt, 1888, vol. 26, pp. 717-731.

16. Professor of psychology and librarian of Harvard-Robbins Library of Philosophy, Emerson Hall, Harvard University.

17. Of the Fatigue Laboratory, Harvard School of Business Administration.

translated in its entirety and will be published soon both in Latin and in English.

I am very happy indeed to be the first to submit the original together with the English translation of the important passage appearing on pages 29 and 30 of Purkyně's published thesis [11] as well as in the unique German "History of Ophthalmology" [18]:

28. Limpiditas vel turbatio corporis vitrei externe ex nigredine pupillae aut integrâ aut nebulosâ cognoscitur, distinctis [19] obliqua inspectione et illuminatione juxta methodos prius adnotatas, quae humori aqueo aut lenti pertinent.

Ast cavum quoque oculi ubi corpus vitreum residet, justa methodo inspicere casu mihi datum est, dum perspiciliis myopum armatus, canis oculum, candelae a tergo ejus e longinquo lucente, eo scopo inquisissem, ut de naturâ splendoris, qui non raro e canum feliumque oculis miro modo promanat, edocerer. En! quoties certa directione oculum caniculi inspexissem, lumen illud percellens apparebat, donec fontem invenirem lumen e cavitate vitri in interna oculi reflexum indeque iterum retroflexum. Eodem statim in hominibus experimento repetito idem phaenomenon oblatum est, pupilla namque integra laeto aurantio colore lucebat. De sede adhuc luminis reflexi in ubio versans oculum artificialem conficiendum curavi, cujus cavum aqua limpida aut diversis gradibus turbida repletum posteriorem parietem simulque liquidi substantiam reflexo lumine referebat.

Jam itaque nulla fere oculi membrana aut substantia interna liquidi, lumini rite reflexo oculoque inspicienti latebit, quae si practici anxiam fere physiologorum inquisitionem spernentes non despicient aut perhorrescent, non sine usu in oculorum Diagnostica invenient.

28. The clearness or turbidity of the vitreous body is recognized from without on lateral illumination and inspection by determining whether the color of the pupil is normal or cloudy according to the previously mentioned methods applying to the aqueous humor and lens.

But I also had a chance to see the interior of the eye where the vitreous body is located when, wearing myopic lenses,[20] with candle light coming from far back, I examined the eye of a dog in order to learn about the nature of the shine which often marvelously emanates from the eyes of dogs and cats. Lo! Whenever I observed the eye of the little dog from a certain direction, that light seemed to be thrown back,[21] until I discovered that the light is reflected from the hollow surface of the lens into the eye and then returned. When the experiment was immediately repeated with human beings the same phenomenon occurred; indeed, the whole

18. Hirschberg, J.: Geschichte der Augenheilkunde, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Berlin, Julius Springer, 1918, vol. 15, pt. 1, chap. 23, pp. 93-95.

19. In his footnote referring to this word, Hirschberg [18] wrote as follows: "The Latin of the great physiologist is more difficult to master than that of the Roman classics. I have tried to translate it word by word without regard to beauty. The word 'promanat' Purkyně has probably coined himself."

20. Purkyně wore concave lenses; his right eye was strongly near sighted, while his left eye was affected by central blindness.

21. Helmholtz' explanation of his discovery was practically identical, as will be seen later. In his translation of this word (percellens), Hirschberg used the term "translucent" with a question mark (?).

pupil lit up in a beautiful orange color. Being still uncertain about the location of the reflected light, I constructed an artificial eye, which I filled with water, either clear or turbid to some degree, and the light shining through revealed both the background and the nature of the fluid.

Thus, from now on practically no membrane or liquid content of the eye will escape the properly reflected light or the scrutinizing eye, and if practitioners, spurning the painstaking inquiry of physiologists, will not disdain or fear this [method], they will find it useful in ocular diagnosis.

Commenting on this passage, Hirschberg,[22] a pupil of Helmholtz, stated:

W o n d e r f u l, indeed, m o s t w o n d e r f u l[23] was this discovery by Purkyně in the year 1823. Even if the Latin of the great investigator does not appear to be perfect, it can nevertheless be well understood, at least by those who have acquired the preliminary education of a physician.

Finding it incredible that such a discovery could have passed unnoticed, I decided thoroughly to investigate all that has been reported about Purkyně in the modern histories of medicine. I found that none of the recent editions by American publishers[24] contain anything relating to the passage quoted. Yet the first four lines on page x of Purkyně's obituary in the *Proceedings of the Royal Society of London*[25] might be interpreted as an allusion to it, for they read:

The inaugural dissertation required of the newly-appointed Professor had for its title: "De examine physiologico organi visus et systematis cutanei." In this dissertation he described the now well-known method of investigating the structure of the retina by the appearance seen after waving a flame beside the eye.

Several older historians, authors of authoritative German reference books,[26] gave Purkyně credit for original work, including his observation of the eyeground. The clearest evidence, however, is found in the ophthalmologic "encyclopedia."[18] This furnishes ample proof of Heidenhain's statement. One medical historian[26a] credited Purkyně also with the principle of ophthalmometry, but Hirschberg did not link Purkyně with the ophthalmometer.

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22. Hirschberg,[18] p. 94.

23. The spacing of the type is Hirschberg's.

24. Garrison, F. H.: An Introduction to the History of Medicine, Philadelphia, W. B. Saunders Company, 1929. Castiglioni, A.: A History of Medicine, translated from the Italian by E. B. Krumbhaar, New York, Alfred A. Knopf, Inc., 1941.

25. Obituary Notices of Fellows Deceased, Proc. Roy. Soc. London **19**:ix-xii, 1871.

26. (*a*) Pagel, J. L.: Handbuch der Geschichte der Medizin, Jena, Gustav Fischer, 1903, vol. 2. (*b*) Pagel, J. L., and Schwalbe, J., in Spemanns historischer Medicinal-Kalender, Berlin, W. Spemann, 1906. (*c*) Baas, J. H.: Die gesichtliche Entwicklung des ärztlichen Standes und der medizinische Wissenschaften, Berlin, F. Wreden, 1896.

HELMHOLTZ' INTRODUCTION OF THE EYE MIRROR

After he had announced the construction of his ophthalmoscope, Helmholtz was universally acclaimed and widely celebrated. From the following excerpt of a letter [27] written to his father on Dec. 17, 1850 [28] (after his first presentation of the eye mirror on December 6), it is seen that Helmholtz had called his instrument originally "invention" and then "discovery":

In regard to time measurements, I have not yet any newer results, but I devoted myself to the construction of new apparatus and to the necessary preliminaries. Aside from that, however, I have invented something [29] during my lectures on the physiology of the sense organs that may possibly be of utmost importance to ophthalmology. Indeed, it was so obvious, requiring no more knowledge than what I had learned about optics in the high school, that it now seems odd that others and myself could have been so dull as not to find it. It is a combination of glasses by means of which it is possible to eliminate the dark background of the eye through the pupil without employing dazzling light and to see at once all the peculiarities of the retina even more thoroughly than one can see the external parts of the eye without magnification because the transparent medium of the eye acts like a lens with a magnifying power of twenty. The blood vessels appear most beautifully with the branching arteries and veins, the entrance of the optic nerve and so forth. Till now, a series of most important eye diseases known collectively as "black cataract" have been "terra incognita" (unknown terrain) because nothing was learned of the changes in the eye either during life or after death. My invention makes the most thorough investigation of the inner structures of the eye possible.

I immediately proclaimed this very precious egg of Columbus before the Physical Society of Berlin as my property, and I am now having constructed such an instrument, which will be easier and more convenient to handle than my previous cardboard pastings.[30] Then I shall examine patients, possibly with the chief of our eye department here, and afterward publish the material.

Of great interest are the flattering letters Helmholtz received from many oculists,[31] among whom was Professor Arlt, of Prague (where Purkyně had already returned from Breslau), and von Graefe, of Berlin, who "was to become later the famous founder of scientific ophthalmol-

27. Koenigsberger, L.: Hermann von Helmholtz, Brunswick, Friedrich Vieweg & Sohn, 1902-1903, vol. 1, pp. 133-134.

28. Curiously enough, Purkyně's birthday, his sixty-third.

29. Helmholtz called it "eye mirror." Ruete in 1852, Coccius in 1853 and Stellwag in 1854 retained this name for their instruments. In 1854 Anagnostakis, a Greek, of Paris, constructed an instrument which he named "ophthalmoscope." This term has been in use since that time, and that period was known as the era of ophthalmoscopy.

30. This brings to mind Purkyně's construction of the perimeter, which will be reproduced in my book, to be published soon.

31. Koenigsberger,[27] vol. 1, p. 136.

ogy" [31] and of the *Archiv. für Opthalmologie*. In his letter von Graefe [32] wrote:

> Last summer I was informed by Professor Brücke, of Vienna, that you had succeeded in constructing an instrument for examination of the retina in the living eye; I had even the satisfaction of learning from the same source a few details about the means you used. Professor Brücke was all the more willing to give me this news in that we had often talked about the possibility of such an instrument and he had told me of an earlier plan, the application of which had failed because of the method of illumination. For Brücke believed that the catoptric and dioptric postulates of the apparatus could be simultaneously realized by placing obliquely a concave lens before the observer's eye. . . . In view of the expected early publication of your work, I have promised to my colleagues Dr. Bowman and Dr. Desmarres, of London and Paris respectively, to send them immediately a sample of your apparatus; particularly the former, who is very much interested in the scientific cultivation of his field and has an extensive practice at the Moorfield's hospital and who will look forward to receiving it as early as possible.

On December 16 of the same year, or one year after the memorable invention, Helmholtz [33] wrote again to his father:

> Eighteen orders for ophthalmoscopes have come in here little by little; so my mechanic does a good business. Among them are four from Holland, one each from Paris, London, Cracow, Prague, Breslau, Bonn, Thübingen and Dorpat and one from Berlin for Dr. Böhm, the adopted son of Johannes Schulze.[34] Similar instruments are made in Berlin by the mechanic Dörffel under the direction of Gräf,[35] son of the surgeon general. Six of them have already been sent out. The others will soon be ready, and the mechanic has made a change in them whereby they are much easier to handle. He is making more than have been ordered, and one will soon be sent together with other articles to New York. So, you see, the matter goes around the world.

As in the case of other discoveries, Purkyně did nothing to introduce his method of examination of the eyeground. This may be explained by the fact "that Purkyně was given more to stimulation of thought and to observation of details than to following up productively what he had thought out and noticed," [14] as well as by his doubt of being able to overcome the then prevailing opposition to physiologic discoveries, a doubt clearly indicated in the last sentence of the Latin passage relating to his ophthalmoscopic method. Helmholtz (fig. 2), on the other hand, traveled widely and demonstrated his mirror in many cities of continental Europe, England and America, although he too had at the beginning many powerful opponents.

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32. Koenigsberger,[27] vol. 1, pp. 136-137.

33. Koenigsberger,[27] vol. 1, p. 138.

34. The chief of the Division of Universities at the German Department of Education. The same Schulze who according to Heidenhain [4] was very favorable to Purkyně.

35. Misspelled in the original source.

Thrice Helmholtz refused Knapp's [36] invitation to come to America: Once on Jan. 5, 1873,[37] once on Sept. 15, 1879 [38] and once in 1893.[39] When Knapp invited him to visit the Chicago World's Fair of 1893 he wrote: [39]

> It would always have been a great attraction for me to know America under her normal and ordinary conditions. But I never could become enthusiastic for great expositions, and I never found that anything important could be learned there that was not already known or that was worth the trouble and excitement connected with it. That is why I have decided not to go to Chicago.

Nevertheless, urged by the government of Berlin to represent German science at the Electrical Congress of Aug. 31, 1893 and granted

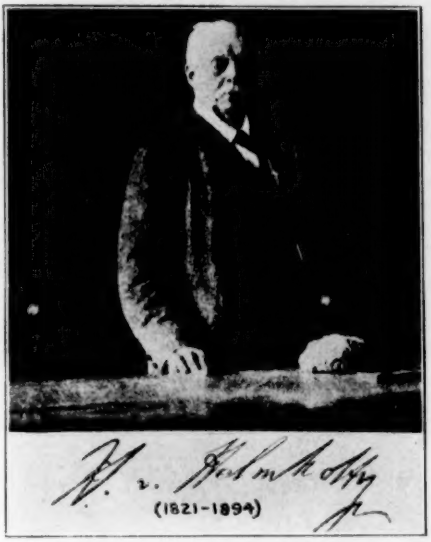

Fig. 2.—Hermann von Helmholtz as he looked shortly after his visit to America. (McKendrick, J. G.: Hermann Ludwig Ferdinand von Helmholtz, New York, Longmans, Green & Company, 1899; reproduced from the frontispiece through the courtesy of the Boston Public Library.)

special permission and an increased allowance for his journey with his wife, he finally consented to go to Chicago, and in his letter addressed to Dr. Knapp on June 20 of that year he announced the date of his arrival in New York and added: [40]

> The final decision was a little difficult, and though I do not feel myself an old man yet, or recognize the various little infirmities of advancing years as any

36. Jacob Herman Knapp (1832-1911), the father of these ARCHIVES and of their present chief editor.

37. Koenigsberger,[27] vol. 2, p. 219.

(Footnotes continued on next page)

serious hindrance, my wife and my friends are somewhat perturbed at my resolution to undertake such a journey in my seventy-second year.

I am convinced that America represents the future of civilized humanity and that it includes a vast number of interesting people, while in Europe we see only the approach of chaos or of a world dominated by Russia.

During his visit in this country Helmholtz traveled widely, giving lectures and demonstrating his ophthalmoscope in many great cities, among which he admired Boston most.

In 1851, or in the same year in which Helmholtz [41] published his monograph about the eye mirror, John Nepomuk Czermak [42] (fig. 3),

Fig. 3.—John Nepomuk Czermak (1828-1873). Reproduced from the frontispiece of the second volume of his collected papers [43c] (courtesy of the Boston Medical Library).

38. Koenigsberger,[27] vol. 2, p. 263.

39. Koenigsberger,[27] vol. 3, p. 71.

40. Koenigsberger,[27] vol. 3, p. 72.

41. von Helmholtz, H.: Beschreibung eines Augen-Spiegels zur Untersuchung der Netzhaut im lebenden Auge, Berlin, A. Förstner, 1851.

42. Czermak, J. N.: (*a*) Ueber eine neue Methode zur genaueren Untersuchung des gesunden und kranken Auges, Vrtljschr. f. prakt. Heilk. **32**:154-165, 1851; (*b*) Beiträge zur Ophthalmoskopie, ibid. **38**:137-141, 1853; (*c*) Das Orthoskop, in Gesammelte Schriften, Leipzig, Wilhelm Engelmann, 1879, vol. 1, pp. 87-101.

Purkyně's first assistant in Prague, described his "orthoscope" (fig. 4) for the examination of the eye. The same Czermak [42d] later introduced the laryngoscope (fig. 5) into medical practice.[43]

The following year (1852) Ruete [44] announced the method of constructing his instrument (fig. 6).

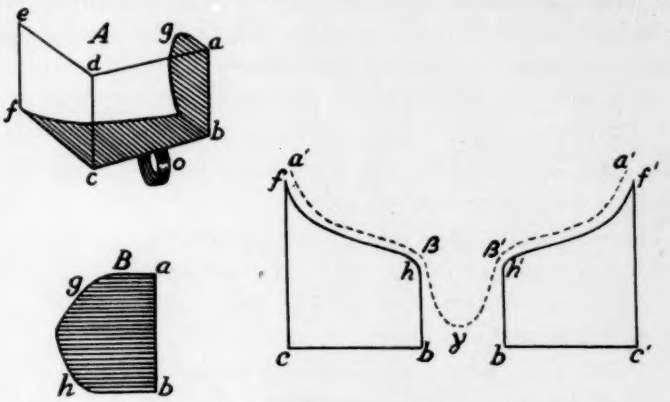

Fig. 4.—Czermak's orthoscope. Reproduced from figures 7 and 8 of the table attached to his original paper on this subject [42d] (courtesy of the Boston Medical Library).

Fig. 5.—Czermak's original laryngoscope. Reproduced from figure 7 (page 26) of his first complete paper on the subject [43b] (courtesy of the Boston Medical Library).

42d. In the spring of 1855, Manuel Garcia (1805-1906), a singer, submitted to the Royal Society of London a report about the successful results he had obtained

(Footnotes continued on next page)

The regular examination of the eyeground with the ophthalmoscope in an upright image (fig. 7) was begun in 1854 by Edward Jäger, who developed with his instrument the art of objective refractive measurements. His ophthalmoscope was provided with twenty-seven lenses and had a fork into which the lenses could be inserted.

The first ophthalmoscopes with circular disks containing corrective lenses for measurement of the refractive error of the observed eye—the so-called refraction ophthalmoscopes—were introduced by Knapp, H. Cohn, Loring and de Wecker in the years 1870 to 1872.

A binocular ophthalmoscope was made in 1861 by Giraud-Teulon of Paris, who adapted to his use a Brewster prism stereoscope behind the hole of a concave mirror.

R. Liebreich was the first to make photographs of the eyeground. He was followed by Dor, of Lyons, 1884; by Star, of Buffalo, in 1887, and then by other investigators. The progress in this phase of ophthalmology was rapid and is still continuing.

Great and many were the honors conferred on Helmholtz for his "discovery." Here are a few examples:

At the ophthalmologic congress in Heidelberg in 1858 he was given a cup on which were inscribed the following words: "To the creator of a new science, to the benefactor of mankind, in grateful remembrance of the invention of the ophthalmoscope."

In a letter [45] to his father dated Dec. 9, 1858 he said: "Professor Donders, of Utrecht, wrote that a new hospital for eye diseases under his direction has been built there and that at its formal opening the

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in trying to see his larynx with a dental mirror bought from Charrière, of Paris. In 1857 Ludwig Türck (1810-1869), a Viennese neurologist, without knowing of Garcia's work, experimented with similar mirrors and occasionally succeeded in seeing the larynx in some of his patients.

It was, however, Czermak (quoted by Pagel,[26a] 1905, vol. 3, pp. 586-588), who perfected an instrument, which he named "laryngoscope" and which he recommended * "for the widest and most general use." In introducing the laryngoscope into general practice, he expressed the hope * that through it "the eye would become a safe guide for the hand." The difficulties of Garcia and Türck were caused by their use of sunlight. Czermak was the first to advise the use of artificial light and to show that his laryngoscope might serve to examine not only the larynx but the pharynx and the rear of the nose and the soft palate. He was also the first to use a frontal mirror with a perforated center.

43. (*a*) Ueber den Kehlkopfspiegel, Wien. med. Wchnschr. **8**:196-198 and 265-268, 1858; (*b*) Der Kehlkopfspiegel, Leipzig, Wilhelm Engelmann, 1860; (*c*) Gesammelte Schriften, ibid., 1879, vol. 2, pp. 76-83.

44. Ruete, C. G. T.: Der Augenspiegel und das Optometer für praktische Aerzte, Göttingen, Dietrich, 1852.

45. Koenigsberger,[27] vol. 1, p. 319.

occasion was considered proper to commemorate the invention of the ophthalmoscope."

On Aug. 9, 1886, at the fifth centenary of the University of Heidelberg, there was another meeting of ophthalmologists. With Professor von Zehender in the chair and in the presence of distinguished visitors, Donders made a brilliant speech and presented Helmholtz with the first of the medals established as a memorial to von Graefe and awarded every tenth year to the man of any nationality who has made the greatest contribution to ophthalmology.

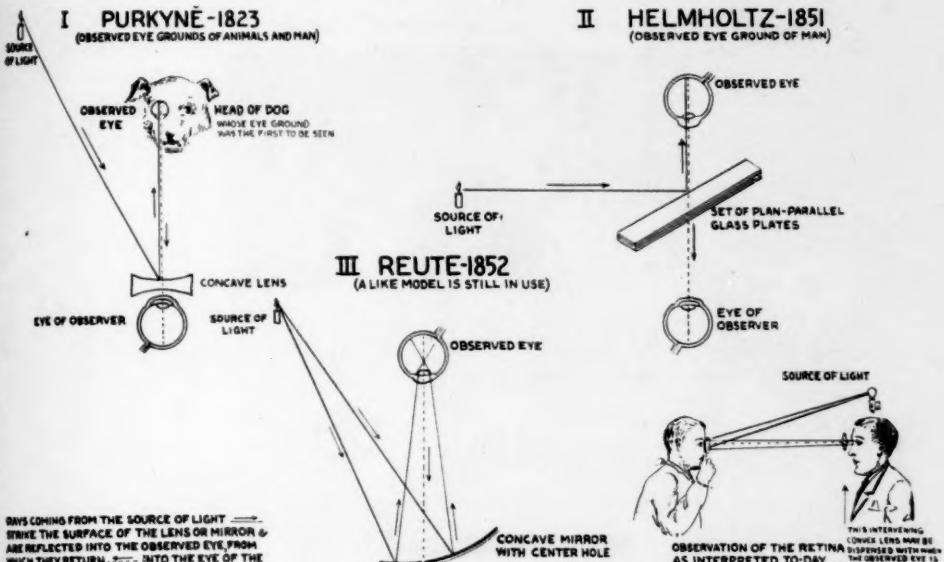
I PURKYNĚ-1823
(OBSERVED EYE GROUNDS OF ANIMALS AND MAN)
SOURCE OF LIGHT
OBSERVED EYE
HEAD OF DOG
WHOSE EYE GROUND WAS THE FIRST TO BE SEEN
CONCAVE LENS
EYE OF OBSERVER
SOURCE OF LIGHT
II HELMHOLTZ-1851
(OBSERVED EYE GROUND OF MAN)
OBSERVED EYE
SOURCE OF LIGHT
SET OF PLAN-PARALLEL GLASS PLATES
EYE OF OBSERVER
III REUTE-1852
(A LIKE MODEL IS STILL IN USE)
OBSERVED EYE
CONCAVE MIRROR WITH CENTER HOLE
EYE OF OBSERVER
RAYS COMING FROM THE SOURCE OF LIGHT STRIKE THE SURFACE OF THE LENS OR MIRROR & ARE REFLECTED INTO THE OBSERVED EYE, FROM WHICH THEY RETURN INTO THE EYE OF THE OBSERVER.
SOURCE OF LIGHT
OBSERVATION OF THE RETINA AS INTERPRETED TO-DAY
INVERTED IMAGE SEEN IN INDIRECT OPHTHALMOSCOPY
THIS INTERVENING CONVEX LENS MAY BE DISPENSED WITH WHEN THE OBSERVED EYE IS STRONGLY MYOPIC

Fig. 6.—Diagrams illustrating the ophthalmoscopic methods of Purkyně,[11] Helmholtz[41] and Ruete.[44] Compare diagram II with figure 4 (page 16) of Landolt, E.: Manuel d'ophthalmoscopie, Paris, Octave Doin, 1878, page 16.

On Helmholtz' seventieth birthday, in 1891, the whole civilized world feted him more than any other scholar has been feted on such an occasion. In an address delivered a year later (on Nov. 2, 1892), he stated:[46]

The ophthalmoscope became the most popular of my scientific achievements, but I have already pointed out to the oculists that good fortune had relatively more to do with it than my merit. I had to explain to my students the theory of emission of reflected light from the eye as discovered by Brücke. Brücke himself was but a hair's breadth away from the invention of the ophthalmoscope. He

46. Koenigsberger,[27] vol. I, pp. 138-139.

had only failed to ask himself what optical image was formed by the rays reflected from the luminous eye. For his purpose it was not necessary at the time to ask this question. Had it occurred to him, he was the man to answer it just as quickly as I did and to invent the ophthalmoscope. I was turning the problem over and over and pondering the simplest way of making it clear [47] to my audience when I came on this question.

The oculist's perplexity in dealing with the condition known at that time as "black cataract" was familiar to me from my medical studies, and I at once set to work to make the instrument by gluing together lenses and cover glasses used for microscopic specimens. At first the instrument was difficult to use. Had I not been theoretically convinced that it must succeed, I might not have persevered but after about eight days I had the great joy of being the first to see a living retina exposed before me.

Fig. 7.—Straight image seen in direct ophthalmoscopy. Reproduced from figure 47 (page 70) of Axenfeld, T.: Lehrbuch und Atlas der Augenheilkunde, ed. 6, Jena, Gustav Fischer, 1920.

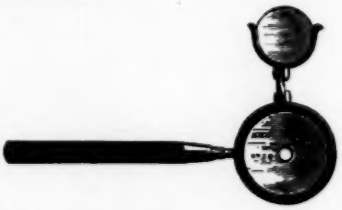

Fig. 8.—Liebreich's mirror, reproduced from figure 50 in Axenfeld, T.: Lehrbuch und Atlas der Augenheilkunde, ed. 6, Jena, Gustav Fischer, 1920. The fork of this mirror, holding the inserted replaceable lens, when in use is turned on its hinge behind the center hole of the mirror.

None of Helmholtz' great achievements in the field of physiologic optics contributed so much to his fame as the introduction of his eye mirror into medical practice. Purkyně, however, who many years before established the principle of ophthalmoscopy, was practically forgotten. The fact that Purkyně was the first to observe the eyeground in animals and in human beings was apparently unknown to Helmholtz and to his

47. His early explanations of the principle underlying his mirror were rather difficult to understand, for even his close friend the great physiologist E. Du Bois-Reymond complained to him once about this in a letter.[27]

great biographer, Prof. Leo Koenigsberger,[27] because no reference to it is found in any of their writings. It seems that even Heidenhain's statement [14] relating to this phase of ophthalmologic research escaped their notice.

Helmholtz, who spoke highly of Purkyně,[48] expressed the latter's thought also in regard to the high standing of the medical profession, as is shown by the following example:

In the second paragraph on page 1 of the introduction to the work [11] in which he announced the method of examination of the eyeground, Purkyně stated:

> It is fitting that a physician discharging such a duty should like above anything else to achieve the reputation of an artist, for prior to that he functions rather as a healer; then he could be compared with Phidias, who designed Apollo and Juno, although the work of a healer seems to require no less inspiration.

In his address delivered in Heidelberg before the ophthalmologic society, Helmholtz,[49] visibly very moved after having received the first Graefe medal, modestly compared himself with a "smith who made a good instrument" and the physician with such artists as Phidias and his successors Praxiteles and Paionios. Helmholtz' wife, who was one of the most cultivated and talented women in Germany and who was a close relative of the famous Hugo von Mohl,[50] reproaching her husband because of the modesty of his speech,[51] wrote:

> Yesterday evening and this morning the papers reported your beautiful but altogether too modest address. Indeed, you are not that "smith" you spoke of, and it was particularly hard for me to think of those "gentlemen" oculists as of so many "Praxiteles" to be compared with you. It was good for those younger gentlemen to hear at least to whom they owe the scientific basis of their specialty. For, as it has seemed to me more than once, they take the eye mirror for something natural and commonplace, just as we do the fork and the knife.

COMMENT

The fact that Helmholtz was the first to devise the eye mirror and to make thereby a great contribution to science is too well known. It is likewise well known that it was that mirror which led directly to the invention and construction of all those instruments which are indispensa-

48. von Helmholtz, H.: Vorträge und Reden, Brunswick, Freidrich Vieweg & Sohn, 1896, vol. 1, pp. 291-292.

49. von Helmholtz,[48] vol. 2, pp. 312-320.

50. Hugo von Mohl (1805-1872), who confirmed Purkyně's botanical findings and who in 1846 introduced into botany (von Mohl, H.: Ueber die Saftbewegung im Inneren der Zellen, Bot. ztg. **4**:73-78 and 89-94, 1846) the term "protoplasm," which Purkyně was the first to use (Übersicht der Arbeiten und Veränderungen der schles. Gesellschaft für vaterländische Kultur, 1839, pp. 81-82).

51. Koenigsberger,[27] vol. 2, p. 341.

ble to the illumination and examination of various body cavities. The head (ear and nose) mirror, the laryngoscope, the bronchoscope, the urethroscope and many other diagnostic aids of that kind produced by progressive and mechanically minded physicians are all based on the same principle.

What is generally not known is the fact that the principle of construction of all those mirrors was established by Purkyně thirty years before Helmholtz had announced the invention of the ophthalmoscope. The words Purkyně used in his announcement of the principle on which his instrument is based are almost exactly repeated in a portion of Helmholtz' address [52] "delivered at the opening of Professor H. Knapp's Clinic at the College of Physicians and Surgeons in New York on October 3, 1893." On that occasion Helmholtz explained the principle of ophthalmoscopy as follows:

> About 1846 the English oculist Dr. William Cumming discovered that the experiment which had succeeded on the luminous eyes of mammals could also be performed on the living eye of human beings and that everybody's eyes could be made luminous.[53] . . . The experiment is very simple. . . . The rays of light pass alongside the head of the observer into the eye of the observed [54] and are reflected back in the direction from which they had proceeded, making the observed eye appear very luminous to the observer.

Even more convincing is the comparison of Purkyně's announcement in the Latin passage heretofore translated with the following portion of Helmholtz' speech:

> The professor described and illustrated by numerous blackboard drawings how with two persons sitting opposite one another the rays of a light placed at the side of one were thrown from a glass plate placed obliquely between the two into the eye of the other and passed through his pupil into the background of his eye. From the background they returned, the way they had traveled before, to the glass plate, which reflected a part of them back to the light whereas another part passed through the glass plate into the pupil of the other person and on reaching his retina made him see the pupil of the first person illuminated. A similar process was observed by a student, Carl von Erlach, after hearing a lecture of Professor Brücke, of Vienna. He was near sighted, and accidentally the light from a gas flame fell on his concave spectacles, was reflected into the eye of a fellow student and made his pupil appear luminous to Erlach.[55]
>
> All that was original with me was that I went on to ask how the optic images could be produced by the light coming back from the illuminated eye. All my predecessors failed to put this question to themselves.[56] They had stopped in the middle of their way instead of going to the end. As soon as I had answered that

52. von Helmholtz, H.: The History of the Discovery of the Ophthalmoscope, M. Rec. **44**:769-772, 1893.

53. Purkyně made the same discovery a quarter of a century before Cumming.

54. Note the light reflex on the side of the observed eye seen in figure 7.

55. This had happened to Purkyně almost a quarter of a century before (only instead of the gas, it was a candle).

56. Purkyně did ask and answer that question correctly.

question I saw how an ophthalmoscope could be constructed, and it took me only two days to construct one and to experiment successfully with it.[56]

There can be no doubt now that Purkyně was the first to announce the principle of ophthalmoscopy,[11] and the best way to prove his priority right to this discovery will be to follow Hirschberg's example [57] by "letting the author, in important matters, speak for himself." To his friend P. G. Tait, in Scotland, Helmholtz [58] wrote as follows: "The real discoverer is he who has had the original idea. Experiments, it is true, are also necessary, but it is easier to institute those than to find the idea, and experiments can be made by anyone else."

CONCLUSION

The purpose of this report is to show that Purkyně was the pioneer in the illumination and examination of the eyeground and consequently the discoverer of the principle of ophthalmoscopy. Nothing is detracted from the credit due Helmholtz for his devising and constructing the eye mirror. On the contrary, it is fully recognized that he put Purkyně's idea to practical advantage and thereby contributed greatly to the practice and the science of medicine. Just as the principle of the radio (Hertz) was known long before Marconi, so the principle of the ophthalmoscope was known before Helmholtz, and just as Marconi's name is always connected with the radio because he put it to practical advantage, so Helmholtz' name is and will always be connected with the eye mirror. Purkyně never exploited any of his discoveries but was always searching for new knowledge and finding it.[14] He could not afford to travel even to satisfy his scientific needs, let alone to introduce his methods. The only trip he ever made was to visit his friend Flourens [59] and to receive an honor from the Academy of Paris. But he did record his findings, because, as a scientist and as one of the truest of Czechs, he believed in that old Slavic proverb

ЧТО НАПИСАНО ПЕРОМЪ,
ТОГО НЕ ВЫРУБИШЬ И ТОПОРОМЪ.

which in English means almost literally

What with a pen has been traced
Can't even with an ax be effaced!

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57. Hirschberg,[18] Vorwort, p. vi.

58. von Helmholtz, H.: Brief on Tait, in Baas,[26c] p. ii.

59. P. Flourens (1794-1867), like Purkyně famous for his investigations of experimental brain lesions and at the time of the latter's visit president of the French Academy of Sciences.

Thus the truth about the origin and development of ophthalmoscopy has been clearly established, and in the words of the founder of these ARCHIVES [60] it may be added that "a truth when once recognized is a truth forever."

485 Commonwealth Avenue.

60. von Helmholtz,[52] p. 770.

CHEMICAL EQUILIBRIUM BETWEEN BLOOD AND AQUEOUS HUMOR

FURTHER STUDIES

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PHILADELPHIA

In 1933 one of us [1] reported on the urea content of aqueous humor and of blood withdrawn simultaneously from the same animal. The concentration of urea in the aqueous humor was found to be about 18 per cent lower than that in the blood stream when equal volumes of fluid were compared. Calculations of the amount of urea per hundred cubic centimeters of water in aqueous humor and in blood showed that the aqueous contains about 25 per cent less urea than the blood. Since the urea in the blood is not bound by the proteins but is free and diffusible, it seemed probable that the membrane separating the two fluids is not inert but shows selective permeability and holds back the urea in the blood stream. The other alternatives are that the urea is destroyed in the anterior chamber after the aqueous has been formed, that the urea is selectively reabsorbed or that additional fluid not containing urea is added to the aqueous in the anterior chamber after it has been formed.

No matter what the explanation of the decreased urea content in the aqueous may be, certainly it is not in accord with the theory of dialysis, as was originally claimed by Duke-Elder.[2] Dialysis may, however, be concerned in the formation of aqueous, for it is possible that the aqueous is primarily formed by dialysis from the capillaries of the ciliary body and that subsequently its chemical composition is so altered by passage

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Read before the Baltimore Ophthalmological Society May 21, 1941.

This work was made possible by a grant from the John and Mary R. Markle Foundation.

From the Department of Ophthalmology of the University of Pennsylvania School of Medicine.

1. Adler, F. H.: Is Aqueous Humor a Dialysate? Arch. Ophth. **10**:11-19 (July) 1933.

2. Duke-Elder, W. S.: Osmotic Pressure of Aqueous Humor and Its Physiological Significance, J. Physiol. **62**:315-329 (March) 1927.

through other membranes, such as the ciliary epithelium, that it no longer resembles a dialysate.

Previous to the appearance of our paper Walker [3] had reported the urea concentration to be 30 per cent less in the aqueous than in the blood serum. A number of other authors, however, have found the urea content of the aqueous almost identical with that of the blood, and in a recent paper Benham [4] claimed further proof of the dialysate theory of the formation of aqueous by the equality in concentration of urea in aqueous and in blood. Finally, an important paper by Duke-Elder, Quilliam and Davson [5] reviewed the subject and offered several possible explanations for the discrepancy. They stated:

> In this connection two circumstances must be borne in mind: (*a*) The possibility that the chemical methods available for the estimation of freely diffusible organic materials are not sufficiently specific, so that comparison between a protein-free and a protein-rich fluid is not warrantable. Thus Benham (1937), using improved chemical methods, found much more consistency in the distribution of urea. (*b*) Where the non-electrolyte is a metabolite its concentration in the aqueous humor and plasma will vary continuously.

It has seemed to us that this question of the urea content of aqueous and of blood is a vital point in evaluating the theory of dialysis, for if the aqueous is formed by dialysis either it must have the same urea content as blood or some explanation for the discrepancy must be found. Accordingly we set ourselves a number of problems, which will be considered seriatim.

METHODS

In all the experiments except as especially noted cats were used and were anesthetized by means of intraperitoneal injections of sodium amytal, 50 mg. per kilogram of body weight.

The method employed for the urea determinations was an adaptation of the standard urease aeration-nesslerization procedure developed by Dr. W. C. Stadie,[6] of the Hospital of the University of Pennsylvania, for use with the Evelyn photoelectric colorimeter. Urea tubes with ground glass stoppers were used, and these were joined with gum rubber tubing in such a way as to form practically glass to glass junctions. One-tenth or two-tenths cubic centimeter samples of serum or aqueous humor were digested with urease, and the ammonia on aeration was

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3. Walker, A. M.: Comparison of Chemical Composition of Aqueous Humor, Cerebrospinal Fluid, Lymph, and Blood from Frogs, Higher Animals, and Man: Reducing Substances, Inorganic Phosphate, Uric Acid, Urea, J. Biol. Chem. **101:** 269-287 (June) 1933.

4. Benham, G. H.: Distribution of Urea in Blood and Aqueous Humor, Biochem. J. **31:**1157-1160 (July) 1937.

5. Duke-Elder, W. S.; Quilliam, J. C., and Davson, H.: Some Observations on Present Position of Our Knowledge of Intra-Ocular Fluid, Brit. J. Ophth. **24:** 421-444 (Sept.) 1940.

6. Stadie, W. C.: Personal communication to the author.

caught in 1 : 300 hydrochloric acid. Aliquots containing 0.01 to 0.035 mg. of nitrogen were nesslerized and the reaction read in the Evelyn colorimeter with the 440 or the 520 filter, depending on the amount of nitrogen in the final solution. Recovery of various amounts of urea from standard solutions averaged 99.5 per cent (+ 1.25); from serum, 100.4 per cent (+ 1.6), and from aqueous humor, 100 per cent (+ 1.25).

All the chemical analyses were performed by Dr. Elinor Moore and were done in duplicate.

I. COMPARISON OF THE UREA CONTENT OF THE AQUEOUS HUMOR OF THE TWO EYES AND OF THE BLOOD IN NORMAL ANIMALS

The samples of aqueous humor were withdrawn from the anterior chamber by means of Luer syringes, care being taken that there was no admixture of blood from any iris vessels which might leak. Approxi-

TABLE 1.—*Comparison of the Urea Content of the Two Eyes*

Animal	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
	Serum	First Eye	Second Eye	First Eye	Second Eye
Dog 1*	22.5	15.7	15.0	69.8	66.7
Cat 1	60.0	55.1	54.4	91.9	90.7
Cat 2	65.6	58.3	56.3	88.8	85.9
Cat 3	57.5	48.6	48.4	84.7	84.4
Cat 7	77.7	65.8	65.2	84.7	84.0

* Ether anesthesia.

mately the same quantity of aqueous was withdrawn from each eye, although it was found that the amount of aqueous did not vary the concentration of urea found.

Table 1 shows the urea content of the aqueous of 4 normal cats and 1 dog and the urea content of the blood serum withdrawn from the femoral artery at the time of the puncture of the anterior chamber. Table 2 shows the urea content of the aqueous and of the blood in 17 cats. It is evident from these tables that the primary aqueous of the two eyes is almost identical in urea concentration, and the average for the 21 cats shows the urea content of the aqueous to be about 80 per cent that of the blood serum. When the figures are corrected for the difference in solids of blood and of aqueous the urea content of the aqueous is found to be about 73 per cent that of serum.

This confirms the work of Walker and our own earlier figures, obtained with an entirely different chemical method.

There can be no question that the methods employed were not sufficiently specific for comparison of urea concentrations in protein-rich

and protein-free fluids, as tests showed the same error in the recovery of urea from solutions which were protein free and in its recovery from those which contained an amount of protein equivalent to that of blood. Further, the error was way below that of the differences we have found between aqueous and blood, being less than 2 per cent.

II. COMPARISON OF THE UREA CONTENT OF PRIMARY AND OF SECONDARY AQUEOUS HUMOR

If the urea concentration in normal aqueous is approximately 25 per cent less than in the equivalent fluid volume of blood, what is the con-

TABLE 2.—*Urea in the Primary and in the Secondary Aqueous Humor*

Cat	Interval Between Primary and Secondary Aqueous, Minutes	Mg. of Urea per 100 Cc.					Aqueous/Serum Percentage		
		Serum 1	Primary Aqueous	Serum 2	Secondary Aqueous	Control Aqueous	Primary Aqueous	Secondary Aqueous	Control Aqueous
22	Continuous Flow	36.2	....	....	35.8	32.3	....	98.9	89.3
23	Continuous Flow	47.4	....	....	42.2	36.3	....	89.1	76.6
24	14	36.2	28.0	33.6	33.9	27.6	77.4	101.0	82.2
18	15	36.3	28.3	37.8	29.3	27.1	78.0	77.5	71.7
20	15	50.5	34.5	50.4	46.6	34.8	68.4	92.6	69.1
19	16	49.4	41.2	50.4	43.1	41.2	83.4	85.6	81.8
15	17	45.1	31.9	44.4	34.7	34.2	70.8	78.2	77.0
17	24	62.6	51.9	62.6	51.8	47.6	82.9	82.8	76.1
16	32	82.3	61.9	84.2	69.6	64.1	75.2	82.7	76.2
14	34	63.2	45.6	63.0	51.4	47.9	72.2	81.6	76.1
12	56	73.5	64.6	70.3	63.7	63.2	87.9	90.6	89.9
8	60	48.1	36.2	44.4	38.8	....	75.3	87.3	....
11	62	90.9	74.3	85.7	74.1	....	81.9	86.5	....
9	70	57.2	43.9	50.9	41.2	....	76.8	81.0	....
10	71	48.3	38.9	46.1	39.1	....	80.6	84.8	....
42	1427	57.5	42.1	50.2	39.7	37.9	73.3	79.2	75.5
43	1441	44.8	36.9	44.4	37.1	34.9	82.4	83.6	78.6

centration of urea in secondary aqueous, which forms when the anterior chamber has been opened and the pressure outside the blood vessels has been reduced to zero? It is well known that so-called secondary, or plasmoid, aqueous more nearly resembles blood in its chemical composition than does primary aqueous, and this is particularly true with respect to protein, which in the primary aqueous is almost nonexistent but in plasmoid aqueous amounts to some 7 or 8 per cent.

Table 2 shows the figures obtained for a series of cats from which the plasmoid aqueous was withdrawn at varying periods after the initial puncture for obtaining the sample of primary aqueous. The time intervals ranged from a period long enough only for the formation of plasmoid aqueous in amounts sufficient to be collected for analysis, and this we have termed "continuous flow," to a period of nearly twenty-

four hours. In every case all the aqueous was withdrawn from the anterior chamber; so there was no admixture of the newly formed plasmoid aqueous with the original primary aqueous.

In order to compare analyses of fluids withdrawn over a considerable period it was necessary to make sure that there had been no change in the blood urea level during that period. Hence a blood sample was taken when the primary aqueous was withdrawn from one eye, and when the plasmoid aqueous was withdrawn a second blood sample was taken. On the whole there was little change in the blood urea level even over a twenty-four hour period.

Since it has been found that the aqueous urea is identical in the two eyes of a normal animal we used the primary aqueous of the second eye as a control, withdrawing it at the same time that the plasmoid aqueous was withdrawn.

It can be seen from the table that the plasmoid aqueous as it is formed approximates blood plasma in its urea content. In a short period, however, the contents of the anterior chamber show a concentration of urea which more nearly resembles that of normal primary aqueous.

This period is so short it proves unlikely that the decrease in concentration is due to ferment action.

III. DETERMINATION OF THE RATE OF INCREASE OF UREA IN THE AQUEOUS FOLLOWING INJECTION OF UREA IN THE BLOOD STREAM

A series of cats received intravenous injections of 5 cc. of 25 per cent solution of urea per kilogram of body weight. This was injected at the rate of 2 cc. per minute into the jugular vein. Samples of blood and of aqueous were withdrawn for analysis from the different animals at varying periods. These periods ranged from three minutes to twenty-four hours.

Table 3 summarizes the findings for 18 cats. Three examples will serve to make clear the interpretation of the figures.

EXAMPLE 1.—From cat 27 a blood sample and the aqueous of the right eye were withdrawn three minutes after the intravenous injection of the urea. The blood serum contained 328 mg. of urea per hundred cubic centimeters, and the aqueous contained 58 mg. The aqueous contained only 17 per cent as much urea as the blood, whereas normally it contains about 80 per cent as much.[7]

This means that when the blood is suddenly loaded with urea there is a definite barrier which does not let urea diffuse rapidly into the aqueous. How effective this barrier is will be seen in the interpretation of the data for the whole series of animals.

7. All the figures given from this point on are not corrected for the differences in solids between blood and aqueous.

A second blood sample was withdrawn at the end of twenty minutes, and at the same time the right eye was emptied of its secondary, or plasmoid, aqueous and the left eye was tapped for its primary aqueous. The level of urea in the blood serum had now fallen to 237 mg., whereas that in the plasmoid aqueous from the right eye had risen from 58 mg. to 210 mg. The level of urea in the primary aqueous from the left eye was now 93.4 mg.

From these values it can be concluded that the rather slow diffusion of urea into the anterior chamber continues for at least twenty minutes even though the blood urea level has started to fall. It is also clear that the secondary aqueous more nearly resembles the blood, just as it does in the normal animal with an undisturbed blood urea level.

TABLE 3.—*Urea Content of the Aqueous Humor After the Injection of Urea*

Cat	Time from End of Injection, Minutes	Mg. of Urea per 100 Cc.		Time from End of Injection, Minutes	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage		
		Serum 1	Primary Aqueous		Serum 2	Secondary Aqueous	Control Primary Aqueous	Primary Aqueous	Secondary Aqueous	Control Primary Aqueous
27	3	328	58.0	20	237	210	93.4	17.7	86.6	39.4
25	5	261	57.1	23	202	193	78.8	21.9	95.6	39.0
26	4	395	62.8	34	261	170	113.0	15.9	65.2	43.3
28	3	339	76.8	36	227	201	127.0	22.7	88.5	55.9
29	4	353	70.5	47	246	211	117.0	20.0	85.8	47.6
30	7	259	91.8	56	193	194	124.0	35.4	100.0	64.3
32	5	245	48.0	65	149	148	84.4	19.6	99.4	56.6
31	5	284	62.5	67	210	194	123.0	22.0	92.4	58.6
33	46	201	95.8	95	181	139	115.0	46.1	76.6	63.3
34	101	153	110.0	163	134	123	112.0	71.9	92.3	84.0
35	92	190	134.0	184	149	135	127.0	70.5	90.7	85.1
36	97	208	154.0	182	176	168	165.0	74.3	95.2	93.4
37	187	123	113.0	364	89.7	87.1	83.8	91.8	97.2	93.5
39	370	95.2	99.0	721	61.7	64.3	60.9	104.0	104.0	98.8
38	423	126	104.0	737	60.4	64.3	59.8	82.9	107.0	99.1
40	424	159	143.0	1091	79.4	78.3	79.1	93.7	98.8	99.8
41	1084	48.3	44.9	1451	47.8	45.2	39.4	93.0	94.6	82.4
44	1103	51.6	52.9	1472	43.4	42.2	38.6	103.0	97.3	89.0

EXAMPLE 2.—The sample of blood and that of primary aqueous from the right eye were withdrawn from cat 36 one hour and thirty-seven minutes after the injection of the urea. The blood urea level was now 208 mg., and since all the cats received the same amount of urea per kilogram of body weight it is safe to assume that the initial blood urea level was approximately the same for all; hence, the blood had lost about 40 per cent of the injected urea in this time. The level of urea in the primary aqueous, on the other hand, had risen to 154 mg. This is 74.3 per cent of the blood urea content, which is about what normal aqueous contains. In a little over an hour, therefore, the blood-aqueous barrier had permitted the aqueous and the blood to equilibrate in the normal fashion, with a falling blood urea level.

Still later, at a little over three hours, a second blood sample was taken, together with the primary aqueous from the left eye and the plasmoid aqueous from the right eye. The level of urea in the serum had fallen to 176 mg., and that in the primary aqueous of the left eye was now 165 mg., showing a still

further slight increase over the figure obtained at an hour and thirty-seven minutes. The level in the plasmoid aqueous likewise was 168 mg., reflecting quite closely the blood urea level.

It can be said, therefore, that in the period between one and three hours the falling blood urea level and the rising aqueous urea level approach each other. The level of urea in the plasmoid aqueous also about equals that in the blood.

EXAMPLE 3.—From cat 44 samples were taken at nearly nineteen hours. The blood urea had fallen to the normal level. The level of urea in the primary aqueous had fallen, but not to the extent the level in the blood had, so that it was still slightly higher than that in the blood instead of around 20 per cent less. Samples taken twenty-five hours after the injection showed the level in the blood dropping farther and now the level in the primary aqueous was coming down to its normal position in respect to the percentage of the blood urea content it contained. The

TABLE 4.—*Effect of Urea Injected with the Ureters Ligated* *

Cat	Minutes After Injection	Serum Urea, Mg. per 100 Cc.	Aqueous Urea, Mg. per 100 Cc.	Aqueous/Serum Percentage
95	37	226	101	44.8
97	152	219	122	55.7
102	310	286	224	78.3
98	393	342	255	74.8
105	453	288	215	74.8
106	583	311	253	81.4
102	542	293	245	83.7
105	570	298	233	78.1
106	708	360	287	79.7
95	1,354	281	221	78.8

* Five cubic centimeters of 25 per cent urea in 1 per cent sodium chloride per kilogram of body weight was injected into the femoral vein.

level in the secondary aqueous also showed its normal percentage of the blood urea content.

From this experiment it can be concluded that after the injection of urea the blood urea level falls rather rapidly from a high peak, reaching its normal in about twelve hours. The level in the primary aqueous rises rapidly and equilibrates with the falling level in the blood in about three hours. It never exceeds the blood level, but after three hours follows closely the changes in blood level. The level in the secondary aqueous followed the course of the level in the blood throughout the experiment.

The fall in the blood urea level after a single intravenous or intraperitoneal injection is due to the rapid elimination of urea by the kidneys. If the ureters are tied off the urea once injected into the blood stream cannot escape. In a series of cats this procedure was carried out. Table 4 gives the results of 10 experiments. The long delay before the level in the primary aqueous reaches the new blood urea level now becomes manifest. It takes from six to nine hours before the level of urea in the primary aqueous reaches the blood urea level.

IV. COMPARISON OF THE UREA CONTENT OF THE AQUEOUS AND OF THE BLOOD AFTER REMOVAL OF THE PARASYMPATHETIC NERVE SUPPLY ON ONE SIDE

In 4 cats the ciliary ganglion was removed from one side, and after complete recovery (one to two months) samples of aqueous from each eye and samples of blood were analyzed for urea. In 2 experiments these analyses were made without any additional urea being thrown into the cat's blood stream. The figures are shown in table 5. There was no difference in the urea content of the two eyes, and the urea content of each eye was about the normal percentage of the blood urea content.

TABLE 5.—*Urea in the Aqueous of Cats with One Ciliary Ganglion Removed*

Cat		Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
		Serum	Eye Operated On	Control Eye	Eye Operated On	Control Eye
73	.....	36.5	33.4	32.4	91.6	88.8
74	.....	37.1	30.3	29.3	81.7	79.0

TABLE 6.—*Comparison of the Two Eyes of Normal Cats After the Intraperitoneal Injection of Urea*

Cat	Minutes After Injection	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
		Serum	Right Eye	Left Eye	Right Eye	Left Eye
68	74	96.1	57.6	58.7	59.9	61.1
72	92	195.2	114.2	116.9	58.5	59.8
77	93	115.3	71.8	70.5	62.2	61.1
70	104	165.8	96.4	98.8	58.2	59.7
76	112	159.3	119.9 (0.4 cc.)	121.9 (0.7 cc.)	75.3	76.5
78	136	142.8	128.6	126.5	90.2	88.7

It can be said that there is no evidence of any parasympathetic control of the blood-aqueous barrier as far as its permeability to urea is concerned. It seemed possible, however, that if such a control were present its effect might have been nullified or masked by some compensating mechanism after the ganglion had been removed for a period of time. Accordingly an intraperitoneal injection of urea was given to all 4 cats and samples taken of aqueous from each eye and of blood after an hour to an hour and a half had elapsed. The urea was given intraperitoneally instead of intravenously, as we wished to save the animals for further experimentation. In order to determine how the effect of an injection of urea given intraperitoneally would compare with the effect of one given intravenously, 6 cats were given the same amount of urea by the intraperitoneal route as had previously been used intravenously. Table 6 gives the figures for these cats, which show that when the blood urea

level is raised the two normal eyes show an equal and simultaneous rise in their urea level.

Table 7 shows the results of the intraperitoneal injection of urea in cats which had previously had the ciliary ganglion removed from one side. It is evident that removal of the parasympathetic nerve supply had no effect on the rise of the aqueous urea level following an increase in the blood urea.

As a result of the denervation, the pupil on the operated side remained widely dilated, the exposed surface of the iris being reduced to a minimum. From this fact it can be concluded that there was no evident effect of the iris itself on the urea content of the aqueous. It is of course true that even though the pupil was dilated there was considerable iris left which might be able to function and exert an effect on

TABLE 7.—*Effect of the Intraperitoneal Injection of Urea in Cats with One Ciliary Ganglion Removed*

Cat	Minutes After Injection	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
		Serum	Eye Operated On	Control Eye	Eye Operated On	Control Eye
75	62	212	104	102	49.1	48.1
69	73	203	91.6	107	45.1	52.5
73	73	226	105	108	46.4	47.8
74	75	285	188	164	66.0	57.6
74	75	184	111	104	60.2	56.8
69	77	197	84.9	92.5	43.0	46.8
74	95	183	105	110	57.4	59.8

the absorption of urea from the anterior chamber. This point could be decided only by completely removing the iris from the eye.

V. EFFECT ON THE UREA CONTENT OF THE AQUEOUS OF BATHING THE CORNEA WITH SOLUTIONS OF VARYING UREA CONCENTRATION

The cornea is a semipermeable membrane through which water and dissolved substances may pass in one direction or the other. Water, for instance, passes readily through the cornea into the anterior chamber but cannot escape in the opposite direction. This is also true of most salts and of oxygen. Carbon dioxide, on the other hand, can escape from the anterior chamber through the cornea but will not pass into the aqueous if the epithelial and endothelial layers are intact.

The low urea content of the aqueous might possibly be due to the escape of urea into the tears. In order to test this possibility the following experiments were performed:

A. In 3 cats the cornea on one side was bathed with normal Ringer's solution for periods of one to two hours. At the end of this time the aqueous of the two eyes was analyzed together with a blood sample.

B. In 4 cats the cornea on one side was bathed for one to two hours with normal Ringer's solution containing a large amount of urea, and the aqueous and the blood were tested for urea.

Table 8 shows the results of these experiments. There was no effect on the urea content of the aqueous when the cornea was bathed with Ringer's solution containing no urea. In other words, it was not found possible further to reduce the concentration of urea in the aqueous when the cornea was bathed with a solution containing less urea than is normally found in the tears. (Most of the figures in the literature give values for the urea of the lacrimal fluid equal to those for the urea of the blood.) On the other hand, it was possible to increase the aqueous urea by bathing the cornea with a 0.9 per cent solution of urea. Urea, like other crystalloids, can pass through the cornea into the aqueous but cannot readily escape from the anterior chamber in the opposite direction.

TABLE 8.—*Effect of Bathing the Cornea with Ringer's Solution and Solutions Containing Urea*

Cat		Bathing Solution	Time of Bathing, Minutes	Mg. of Urea per 100 Cc.	
				Bathed Eye	Control Eye
72	.....	Ringer's	68	38.7	37.6
68	.....	Ringer's	110	34.0	33.8
68	.....	120 mg. of urea per 100 cc.	121	37.7	37.2
72	.....	0.9 per cent urea	108	37.7	32.7
68	.....	0.9 per cent urea	134	54.3	43.0

It seems unlikely therefore that the low aqueous urea content is due to any loss of this substance through the cornea.

VI. EFFECT OF PROTOPLASMIC POISONS ON THE UREA CONTENT OF THE AQUEOUS

A few experiments were done by injecting various poisons into the vitreous and after varying periods analyzing the urea of the two eyes and of the blood serum withdrawn simultaneously.

Table 9 shows that the injections resulted in no change in the urea content of the experimental eye.

VII. AQUEOUS UREA CONTENT IN SYMPATHECTOMIZED CATS

In a series of cats the right superior cervical ganglion and the right vagus nerve were resected and a comparison made of the aqueous urea content of the two sides after several months had elapsed.

Table 10 shows that the effect was entirely negative. In a second series of cats so operated on a solution of urea was injected intra-

TABLE 9.—*Effect of Poisons on the Urea Content of the Aqueous*

Cat	Poison	Time of Action of Poison, Minutes	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
			Serum	Experimental Eye	Control Eye	Experimental Eye	Control Eye
+79	0.2 cc. of 1:50 iodoacetic acid	47	....	62.4	59.2	....	....
+82	Neutralized iodoacetic acid, 0.2 cc. of a 0.005 molar solution	71	67.7	59.4	55.5	87.8	82.0
++70	Sodium arsenate, 0.2 cc. of a 0.01 molar solution	108	45.0	42.1	42.4	93.6	94.3
80	Sodium cyanide	60	56.0	43.1	42.8	77.0	76.6

TABLE 10.—*Urea in the Aqueous of Sympathectomized Cats*

Cat		Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
		Serum	Aqueous on Right	Aqueous on Left	Aqueous on Right*	Aqueous on Left
89	.....	42.4	35.6	35.2	84.1	83.1
90	.....	33.3	29.9	30.0	89.8	90.2
103	.....	38.2	29.5	27.9	77.3	73.1

* Right side operated on.

TABLE 11.—*Urea in the Aqueous of Sympathectomized Cats After the Injection of Urea* *

Cat	Minutes After Injection	Mg. of Urea per 100 Cc.			Aqueous/Serum Percentage	
		Serum	Aqueous on Right	Aqueous on Left	Aqueous on Right	Aqueous on Left
103	41	224	92.5	90.2	41.2	40.2
89	82	224	144	124	64.2	55.5
90	138	176	129	130	73.2	74.1

* The superior cervical ganglion and the vagus nerve were removed on the right side. The animals were given 5 cc. of 25 per cent urea in 1 per cent sodium chloride intraperitoneally.

TABLE 12.—*Urea Content of the Blood Serum and the Aqueous in a Human Being*

	Mg. of Urea per 100 Cc.	
	Blood Serum	Aqueous Humor
1:45 p.m.	33.7	....
2:15 p.m.	62.1	....
2:45 p.m.	89.3	....
3:15 p.m.	96.5	....
3:45 p.m.	96.5	55.6

peritoneally and after varying periods the aqueous of both eyes analyzed. In 2 of the 3 cats, as shown in table 11, no change from the normal was found. In cat 89 the urea level on the sympathectomized side was higher than that on the normal side. We have no explanation for this, but since we were unable to repeat this finding we believe that it was probably an experimental error.

VIII. COMPARISON OF THE UREA CONTENT OF THE AQUEOUS AND OF THE BLOOD IN HUMAN EYES

We had the opportunity of obtaining aqueous humor from an eye which had to be enucleated because of a melanocarcinoma of the conjunctiva. The eye was normal in other respects and showed no evidence of inflammation. On May 4, 1939 a sample of blood serum showed a urea content of 34.2 mg. per hundred cubic centimeters. The aqueous urea content was 30 mg. per hundred cubic centimeters, or 87.8 per cent of the blood urea content, these figures corresponding closely to those for the cats.

On May 8, 40 mg. of urea was given by mouth to the patient at 1:45 p. m. Blood samples were withdrawn at various periods until the urea had apparently reached its maximum. The aqueous humor was then withdrawn from the eye. The results of the analyses are shown in table 12.

There seems to be no difference between human beings and cats in respect to the level of urea in the aqueous and that in the blood and their equilibration with changes in the blood urea level.

COMMENT

We have confirmed our previous work on the concentration of urea in aqueous and in blood serum using a different chemical method. Control experiments proved the method to be reliable in determining with an error of less than 2 per cent the concentration of urea in solutions containing no protein or containing an amount of protein equal to that of blood.

The normal aqueous humor of cats contains a content of urea about 80 per cent of that of the blood serum when equal volumes are compared. If the figures are corrected for the difference in solids of blood and of aqueous the content of urea in the aqueous is found to be about 73 per cent that in the blood serum.

When the anterior chamber of the cat is evacuated the plasmoid aqueous as it is formed contains approximately the same amount of urea as the blood serum, but within a short time it begins to resemble primary aqueous. This return to the normal is so rapid that it can hardly be accounted for either by a breaking down of the urea by ferments in the anterior chamber after the aqueous is formed or by

selective reabsorption of urea from the anterior chamber. It seems more likely that the permeability of the blood-aqueous barrier to urea is in some way determined by the pressure relationships inside the eye. When the normal intraocular pressure balances the intracapillary pressure in the eye the aqueous as it is formed contains nearly 20 per cent less urea than the blood serum. When, however, the intraocular pressure falls to zero and the intraocular capillaries dilate, urea as well as protein is let through into the aqueous in an amount equivalent to that in the blood. As soon as the intraocular pressure begins to return with closure of the puncture wound the permeability to urea as well as to protein approaches that in the normal animal.

Injections of urea into the blood stream cause a rise in the level of urea in the primary aqueous, but this is not immediate. When a single injection of urea is given into the blood stream in a normal animal the blood urea level immediately starts to fall, as the urea is eliminated rather rapidly by the kidneys. Under this condition it takes from one to three hours for the level of urea in the primary aqueous to equilibrate with a falling blood urea level. The level of urea in the plasmoid aqueous, on the other hand, equilibrates rapidly with the blood urea level.

If the ureters are tied off so that the urea cannot escape from the blood, there is a long delay—from six to nine hours—before the level of urea in the primary aqueous reaches the new blood urea level.

No evidence could be obtained of any influence of the sympathetic or of the parasympathetic nervous system on the blood-aqueous barrier as far as the passage of urea across this barrier is concerned.

Bathing the cornea with solutions containing less urea than that found in normal aqueous did not affect the urea content of the aqueous in any way. Hence, the low concentration of urea in the aqueous cannot be due to loss of urea into the tears. If, however, the cornea is bathed with a solution containing more urea than occurs in normal aqueous, the urea penetrates the cornea and appears in the normal aqueous.

CONCLUSIONS

Under normal conditions the aqueous as it is formed contains less urea than the blood stream. This is due to a lack of permeability on the part of the blood-aqueous barrier, which breaks down if the intraocular pressure is reduced to zero. The barrier is effective for a period in preventing increases in blood urea from reaching the aqueous, for it takes over seven hours for the aqueous urea to equilibrate with the blood urea when this is artificially increased and maintained at a new high level.

No evidence was obtained of any nervous mechanism controlling the blood-aqueous barrier as far as any secretion of urea is concerned.

OCULAR DISTURBANCES IN A CASE OF ACROMEGALY COMPLICATED BY DIABETES

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The following case is interesting from both an ophthalmologic and an endocrinologic point of view.

When the patient, a man aged 35, came to the university ophthalmic clinic of Istanbul on April 16, 1939 he was almost blind.

He was 183 cm. tall (over 6 feet), had some exophthalmos (according to the exophthalmometer of Hertel, 23 mm. at 110) and was a definite acromegalic type. The examination and the history indicated a tumor of the pituitary gland. He suffered from polyphagia and polyuria; in addition, the libido and the sexual potency had completely disappeared, and roentgenograms revealed a greatly enlarged sella turcica. The patient stated that he had had an illness with fever four months before and that sugar had been found in his urine at that time.

The vision of each eye was reduced to perception of movements of the hand. The ophthalmoscopic examination showed neither discoloration of the optic nerve nor diabetic retinitis but definite retinal lipemia. The visual field of the right eye could not be measured; of that of the left eye a small area in the upper nasal quadrant remained (chart 1). The pressure in the retinal arteries was 40 mm. of mercury on each side (Bailliart's dynamometer being used), and the systemic blood pressure corresponded to the age.

Values for the sugar and the fat content of the blood are shown in the following tabulation:

	April 24, 1939 Mg./100 Cc.	May 10, 1939 Mg./100 Cc.	May 27, 1939 Mg./100 Cc.
Total fat, 6,800 (normal, 400)		6,400	3,840
Cholesterol, 708 (normal, 150-200)		628	490
Blood sugar, 392 (normal, 100)		442	370

In the urine there was 3.3 Gm. of sugar per hundred cubic centimeters, with no increase in nitrogenous substances. The basal metabolic rate was normal.

On April 22 the patient was transferred to the hospital for the treatment of internal diseases (Prof. Dr. Nesat Omer).

On April 25 the urine contained 3 Gm. and the blood 300 to 400 mg. of sugar per hundred cubic centimeters.

On April 27 treatment was started with 40 units of insulin, the dose being increased in the next few days to 100 units. In addition, a "sugar diet" was ordered (only 232 Gm. of carbohydrate, in the form of potatoes).

Read before the New England Ophthalmological Society April 15, 1941.

By May 5 the patient's general health had improved, as had his color. The vision was 1/25 in the right eye and 5/35 in the left. There was definite improvement in the visual field. The blood and urine, however, were unchanged.

On May 8 the patient was happy—laughing and whistling. Besides the insulin, injections of posterior pituitary extract were given. The weight was 76.9 Kg.

By May 18 the general improvement had progressed further, as had the improvement in the eyes. The vision on each side was now 5/10. The visual fields are shown in chart 2.

The sugar content in the urine, however, was not influenced.

While it was only 1.7 Gm. per hundred cubic centimeters on May 15, it was again 3.2 Gm. on May 17. Ophthalmoscopically the eyes appeared normal; so a person who did not know of the hyperlipemia could not detect anything unusual.

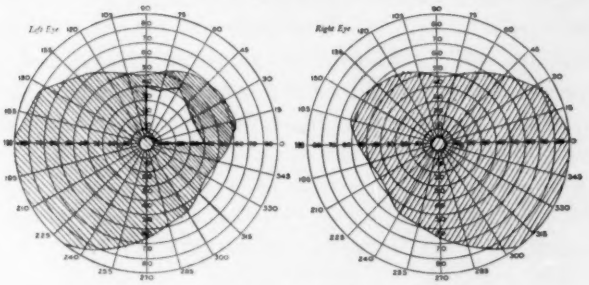

Chart 1.—The visual fields on April 19.

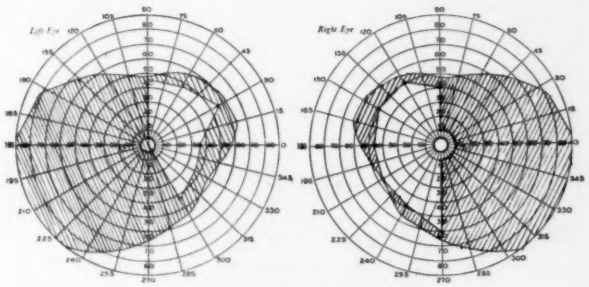

Chart 2.—The visual fields on May 18.

On May 20 the insulin treatment was stopped, and thereafter only pituitary extract was given.

On May 31 the patient again felt badly; also, the vision had decreased in the left eye to 5/20 and in the right eye to 5/6. The visual fields had deteriorated, as shown in chart 3. The sugar content in the urine varied between 2.3 and 3.1 Gm. per hundred cubic centimeters. The blood contained 3,840 mg. of lipid substances, 490 mg. of cholesterol and 370 mg. of sugar per hundred cubic centimeters.

On June 3 all internal treatment was stopped.

On June 12 the vision was found to have decreased to 5/10 in the right and 5/35 in the left eye. There was typical bitemporal hemianopia, and the weight had fallen to 75 Kg.

By June 14 the patient was feeling worse and worse. The vision was 5/20 in the right eye and 1/10 in the left. Ophthalmoscopically, retinal lipemia was to be seen, as in the beginning. Between June 6 and 13 sugar was found in the urine in the same quantities as before.

On June 13 roentgen irradiation of the pituitary gland was begun. On June 25 the vision was 5/7 in the right eye and 5/20 in the left. Bitemporal hemianopia was present. The patient felt very fit.

On July 11 the vision was 5/7 in the right eye and 5/15 in the left. The field was unchanged. Occasionally the patient thought he saw something in the temporal portion of the field. The retinal lipemia had again disappeared.

The patient looked much older than his 35 years. As stated, he said that sugar was found in his urine when he had an infectious disease (grip?) four months before. This diabetes had not been treated. He came by foot and without help to the outpatient department. There was no comatosis, and the general condition was not serious. His psychic depression probably was due to his general disease but could have been

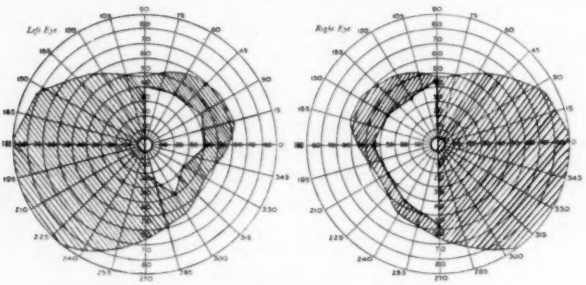

Chart 3.—The visual fields on May 31.

caused partly by the great visual disturbance. He could make no statement as to the beginning of the acromegaly Later on, when he was better, he said that a state of increased sexual desire had preceded his sexual apathy and impotence, as sometimes happens in acromegaly.

It has been known for a long time that acromegaly can be complicated by glycosuria or real diabetes, even with coma. Clinical statistics about the frequency of these complications run from 9 per cent (Arnold) to 35 per cent (Borchardt [1]). Cushing and Davidoff [2] expressed agreement with Hansemann [3] that real diabetes is present in about 12 per cent of cases of acromegaly. In contrast to the older belief that acromegaly is the only pituitary disease with a potential diabetic complication, it is now known that diabetes also may accompany Cushing's

1. Borchardt, L.: Ztschr. f. klin. Med. **66**:332, 1908.

2. Cushing, H., and Davidoff, L. M.: Studies in Acromegaly: IV. The Basal Metabolism, Arch. Int. Med. **39**:672 (May) 1927; V. Disturbances of Carbohydrate Metabolism, ibid. **39**:751 (June) 1927.

3. Hansemann, D.: Berl. klin. Wchnschr. **34**:417, 1897.

disease at least. It seems to be characteristic to a certain degree that in pituitary diabetes hyperglycemia and hypoglycemia alternate without any treatment (e. g. in Goldschmidt's [4] case).

The relationship between the pituitary gland and diabetes has been clarified in the last fifteen years, especially by the experimental work of Cushing and co-workers, Houssay and his school, Young and others.

Diabetes is, as is now known, by no means an endocrine abnormality of only one gland, although the pancreas plays by far the most important role. Overaction of other ductless glands, especially the pituitary, can cause true diabetes. By the work of Houssay and others the antagonism of the islet apparatus of the pancreas and the anterior lobe of the hypophysis was established. Whether the posterior lobe also raises the blood sugar and antagonizes the action of insulin is still doubtful. But it seems almost certain that there are regulating centers for carbohydrate and fat metabolism in the hypothalamus.

Between the growth hormone and the diabetogenic substance there exists according to Houssay a definite intimate relationship.

The main experimental results of Houssay [5] and of others are as follows: After removal of the pituitary, especially in fasting animals, the blood sugar content declines rapidly, and sometimes fatal hypoglycemia occurs. An intake of sugar may save life. According to research the pancreas, the thyroid and the adrenal glands have nothing to do with this kind of hypoglycemia. The animal reacts excessively to an injection of insulin, but the effect can be antagonized by means of pituitary extract. Secondly, anterior lobe extract when injected into animals for a longer period produces glycosuria and ketosis, but there is also an increase in the amount of cholesterol and of lipid substances in the blood, and a greater resistance against insulin can be noted. This total effect is called the "Houssay effect" by Anselmino.[6] Thirdly, removal of the pituitary in diabetic animals improves the clinical state remarkably; hyperglycemia as well as glycosuria and ketosis may practically disappear. These surprising results, said Wright,[7] "suggest that the impaired ability to use glucose or to store glycogen which is characteristic of the diabetic animal depends not only on the absence of insulin, but also on the positive presence of the pituitary."

Young [8] emphasized that the diabetes created by the anterior lobe extract differs from the pancreatic diabetes in that the animals retain

4. Goldschmidt, E.: Schweiz. med. Wchnschr. **65**:766, 1935.

5. Houssay, B. A.: Internat. Physiol. Cong., Zurich, 1938.

6. Anselmino, K. J.: Internat. Physiol. Cong., Zurich, 1938.

7. Wright, S.: Applied Physiology, ed. 6, New York, Oxford University Press, 1936.

8. Young, F. G.: Lancet **2**:372, 1937.

their weight, are in good general health and possess a high resistance against insulin.

These are just the signs found in the case reported, i. e., evidence of involvement of the anterior lobe of the pituitary, a considerable resistance against insulin (as far as the diabetes was concerned) and relatively good general health.

But according to the latest research it is probable that even in the diabetes of pituitary origin the pancreas is the cause of the diabetic condition. Anselmino, Herold and Hoffmann [9] spoke in 1933 of a "pancreatropic" action of the anterior lobe of the pituary. In 1938 Young [10] produced with high doses of anterior lobe extract a permanent diabetes in dogs and found no obvious histologic changes in the thyroid, adrenal and pituitary glands but definite changes in the islets of Langerhans. In 1938 Campbell and Best [11] observed a prompt and extensive fall in the insulin content of dogs' pancreases after injection of a diabetogenic extract of the anterior lobe of the pituitary. Permanent diabetes was produced by seventeen to thirty injections of the extract. During most of this time adequate does of insulin were given, but there was no evidence of recovery of the insulin content in the pancreas (Best, Campbell and Haist [12]). Young [10] said:

> It is conceivable that a short period of hyperactivity might result in the liberation of such excessive amounts of diabetogenic principle as to induce those irreversible changes in the islets of Langerhans which result in the establishment of a permanently diabetic condition. If this is so, then we may have to seek the primary cause of many cases of human diabetes in the anterior lobe of the pituitary gland, rather than in the islets of Langerhans of the pancreas, although defective insulin production by the pancreatic islets may be the secondary and direct cause of the condition.

There is still the great resistance against insulin which is the criterion for an involvement of the pituitary. Very high amounts of insulin, hundreds of thousands of units daily, may perhaps control the glycosuria (Young).

The pituitary's relation to the fat metabolism is not as clear as its relation to the carbohydrate metabolism. Raab,[13] Anselmino and Hoffmann,[14] Houchin and Turner [15] and others have stated definitely that

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9. Anselmino, K. J.; Herold, L., and Hoffmann, F.: Klin. Wchnschr. **12**: 1245, 1933.

10. Young, F. G.: New England J. Med. **221**:635, 1939.

11. Campbell, J., and Best, C. H.: Lancet **1**:1444, 1938.

12. Best, C. H.; Campbell, J., and Haist, R. E.: J. Physiol. **97**:200, 1939.

13. Raab, W.: Klin. Wchnschr. **13**:281, 1934.

14. Anselmino, K. J., and Hoffmann, J.: Klin. Wchnschr. **10**:1438, 1931; Endokrinologie **17**:1, 1936.

15. Houchin, O. B., and Turner, C. W.: Endocrinology **24**:638, 1939.

substances secreted by the pituitary influence the fat metabolism, but this opinion is not yet generally accepted.

In the case reported there was pronounced general hyperlipemia but no (or slight) ketonemia or ketonuria. This state occurs also in ordinary pancreatic diabetes. Jaffe and Schonfeld [16] said: "Why ketosis develops in one case of diabetes and lipaemia in another and why retinal lipaemia develops in so few cases of the latter are unsettled questions."

Katsch and Krainick [17] pointed out that the kind and the degree of the disturbance in fat metabolism are not in harmony with the seriousness of the (pancreatic) diabetes. They expressed the opinion that lasting hyperlipemia in a diabetic person results from a primary central hormonal regulatory disturbance of the lipid metabolism. The possibility that this is true seems to be strengthened by the case reported.

Apparently mine is the first published case of retinal lipemia in "pituitary" diabetes, and its peculiarities raise interesting questions.

The ophthalmoscopic picture was characteristic. The retinal vessels looked as though they had a milky fluid in their lumens instead of blood, and it was difficult or impossible to differentiate arteries and veins.

The retinal lipemia improved and disappeared during treatment with insulin and by diet (posterior lobe extract was given after improvement had already started), although the blood sugar did not decrease. This shows again that retinal lipemia is to a high degree independent of the amount of sugar in the blood. In the preinsulin era McGuire [18] published a case in which the retinal lipemia disappeared whereas the blood sugar increased. The suggestion of Parker and Culler [19] that there is no retinal lipemia without acidosis of the blood is not tenable.

General hyperlipemia and retinal lipemia are of course connected but not as closely as one would think. There are many cases of general and severe hyperlipemia without retinal involvement. On the other hand, retinal lipemia occurs and disappears in the presence of a disproportionate amount of fat in the blood. The retinal disease does not appear before the total blood fat content is 3 Gm. per hundred cubic centimeters (normal, 400 to 600 mg.). In many cases the fat content is much higher, going as high as 20 or even 40 Gm. The amount of cholesterol in the blood is generally increased to 400 to 800 mg. per hundred cubic centimeters and sometimes is 2,000 mg. or more (Allen and Howard [20]). But it is not true that retinal lipemia exists in most cases of general hyperlipemia in which the lipid content is over 5, 6

16. Jaffe, M., and Schonfeld, W. A.: Lipemia Retinalis Due to Diabetes Mellitus, Arch. Ophth. **9**:531 (April) 1933.

17. Katsch, G., and Krainick, H. G.: Klin. Wchnschr. **18**:436, 1939.

18. McGuire, H.: Am. J. Ophth. **5**:862, 1922.

19. Parker, W. R., and Culler, A. M.: Am. J. Ophth. **13**:573, 1930.

20. Allen, J. H., and Howard, W. A.: Am. J. Ophth. **19**:645, 1936.

or 10 Gm. per hundred cubic centimeters (McCann,[21] Ferber and Apperman,[22] McKee and Rabinowitsch [23] and others). There have been cases in which the fundus changes disappeared when the fat content in the blood decreased but was still 13 Gm. (Köllner [24]) or even 16.3 Gm. (Jaffe and Schonfeld [16]); in other cases the changes did not disappear unless the fat content in the blood was below 3 Gm. and reappeared when this content increased to a little higher than 3 Gm. (Lepard [25]). Muskat [26] even mentioned a case in which there was an increase of blood fat coincident with the disappearance of the lipaemia retinalis. In a case reported by Elschnig [27] the retinal lipemia disappeared together with the general hyperlipemia after treatment with insulin, but whereas the general hyperlipemia recurred several times over a period of three years, the retinal lipemia never came back. The patient reported on here had at the beginning of observation (April 24) 6.8 Gm. of total fat per hundred cubic centimeters of blood. When the retinal picture was clearing the lipid content was but slightly changed (6.4 Gm. on May 10), and when a relapse of the retinal lipemia occurred the lipid content of the blood was much less than at the beginning (3.84 Gm. May 27). There is no real explanation as yet for such irregularities.

The clinical picture as well as the development of the condition and its relationship to the sugar and the fat in the blood are about the same in the case here reported, in which the origin was pituitary, as in cases in which the origin is apparently pancreatic. The difference becomes obvious, however, when one considers the visual functions and the reaction of the disease to treatment. On April 27 a "sugar-free" diet and treatment with insulin were started; in a week there was already excellent improvement in the general condition of the patient, some central vision had returned and the retinal lipemia had begun to recede. A week or ten days later the retinal changes had completely disappeared and the visual acuity was 5/10 in each eye; the nasal parts of the visual field were normal, whereas the temporal parts remained blind during the whole observation. The patient was gay and had a much better color, and his much improved condition was apparent. But the sugar had not decreased either in the blood or in the urine; the neutral fat content of the blood, as well as the cholesterol content, was also about the same on May 10 as on April 24. Still more strange is the following circumstance: On May 20 the insulin treatment was stopped.

21. McCann, W. S.: Bull. Johns Hopkins Hosp. **34**:302, 1923.
22. Ferber, J., and Apperman, I.: M. J. & Rec. **125**:815, 1927.
23. McKee, S. H., and Rabinowitsch, I. M.: Canad. M. A. J. **25**:530, 1931.
24. Köllner, H.: Ztschr. f. Augenh. **27**:411, 1912.
25. Lepard, C. S.: Am. J. Ophth. **16**:12, 1933.
26. Muskat, I.: Am. J. Ophth. **7**:288, 1924.
27. Elschnig, A.: Internat. ärztl. Fortbild.-Kurs, Karlsbad, 1929, p. 158.

Posterior pituitary extract was given till June 3, and then all internal treatment was stopped. Within a few days after insulin was discontinued the patient felt much worse and the central vision had decreased, whereas the general hyperlipemia was considerably less on May 27 than two weeks before. The visual acuity decreased more and more and the retinal lipemia relapsed. I think this is really surprising and interesting, but the last stage observed was the most puzzling. It was desired to find out whether the bitemporal hemianopia, probably due to a pituitary adenoma (acromegaly), would react to a roentgen ray treatment. It did not react (at least not in a definite way), but the patient did feel well again, the retinal lipemia disappeared and the vision increased almost to the level at which it had been after the treatment with insulin.

The following questions arise:

1. What was the cause of the patient's blindness?

2. Why were the visual functions so favorably influenced by insulin although the "pituitary" diabetes was so resistant to the pancreatic hormone?

3. How could the insulin and the roentgen ray treatment have had almost the same favorable effect on the retinal condition as on the central vision?

I am not able to answer all these questions satisfactorily, but I want to submit an attempt at explaining some of them.

It is easy to understand that there was bitemporal hemianopia as a result of the pressure of a pituitary tumor. It is unlikely that this pressure had been present for a long while, because there was no optic nerve atrophy. I think that this bitemporal hemianopia could have been improved later by a second roentgen ray treatment, but the patient was satisfied and not sufficiently cooperative.

The bitemporal hemianopia was not influenced by internal therapy. It was present throughout observation of the patient but was not noticeable in the beginning because on it was superimposed a second disturbance, in which the central vision and the visual field as a whole were involved. It is unlikely that only the nasal parts of the field suffered from a process which was the cause of the second disturbance. There would be no way to explain such a binasal hemianopia. It is also unlikely that the second disturbance of the ocular apparatus was produced by the tumor itself, because the involvement of the uncrossed chiasma fibers generally follows much later; the absence of optic nerve atrophy and the quick success of the internal therapy do not favor such an assumption.

The easiest way to understand the second disturbance would be to assume that the retinal lipemia had, because of insufficient nourishment,

a bad influence on the retinal tissue. Reis [28] in 1903 made such a suggestion, but his case was probably complicated by optic nerve disease. Later nobody pointed out that retinal lipemia could produce a functional disturbance. I have studied all the published cases of retinal lipemia without coma and have found that in some of those apparently without complications there actually existed blurred vision or a real decrease in acuity (Darling,[29] 1912; Rowe,[30] 1923; Ferber and Apperman,[22] 1927, and Machlis,[31] 1924). Machlis' patient suffered from diabetic coma with retinal lipemia; when he awoke from the coma, he was "virtually blind," but later the retinal lipemia disappeared, with a full return of the visual capacity. Interesting as this case is, it was complicated by transient coma and cannot be compared with the case here reported. No doubt most patients with characteristic hyperlipemia which could be tested more or less accurately had normal functioning (Turney and Dudgeon,[32] 1906; Köllner,[24] 1912; Moore,[33] 1915; Hardy,[34] 1921; McGuire,[18] 1922; Wagener,[35] 1922; McCann,[21] 1923; McKee and Rabinowitsch,[23] 1931; Chase,[36] 1931, and Jaffe and Schonfeld,[16] 1933). Recently Dr. H. McKee, of Montreal, observed a case (unpublished) very carefully because he knew that I was interested in this condition, and he again found normal functioning.

It is true that in the case reported the improvement of the retinal functioning was simultaneous with the disappearance of the retinal lipemia and that the decrease in vision after discontinuance of the insulin was accompanied by a relapse of the retinal changes. Nevertheless, I cannot believe that the functional disturbance was produced by the hyperlipemic state of the retinal vessels, for the following reasons: It is unlikely that this state in most cases does no harm to the retinal tissue and in other cases does harm. There is no microscopic proof that even extreme hyperlipemia damages the retina or tissue elsewhere. Besides, the good therapeutic effect of roentgen ray treatment is not understandable if one assumes that the visual disturbance is caused by retinal disease.

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28. Reis, W.: Arch. f. Ophth. **55**:437, 1903.

29. Darling, C. G.: Arch. Ophth. **41**:345, 1912.

30. Rowe, A.: Effect of Insulin in Treatment of Diabetic Lipemia with Lipemia Retinalis, J. A. M. A. **82**:1168 (April 12) 1924.

31. Machlis, S. A. D.: Diabetes Mellitus Complicated by Lipemia Retinalis and Xanthoma Diabeticorum, J. A. M. A. **83**:1428 (Nov. 1) 1924.

32. Turney, H. G., and Dudgeon, L. S.: J. Path. & Bact. **11**:50, 1906.

33. Moore, E. F.: Lancet **1**:366, 1915.

34. Hardy, W. F.: Tr. Am. Ophth. Soc. **19**:229, 1921.

35. Wagener, H.: Am. J. Ophth. **5**:521, 1922.

36. Chase, L. A.: Diabetic Lipemia Retinalis, J. A. M. A. **97**:171 (July 18) 1931.

It seems to me more likely that the effect of each kind of treatment (insulin and roentgen ray) was due to the influence on the pituitary-diencephalic region. Whether there was a direct influence on a center in the gland or in the hypothalamus or whether there existed a hydrocephalus of the third ventricle or an overfilling of the cisterna chiasmatis, with indirect pressure on such centers, I do not know. I think one can be fairly sure that the improvement at the beginning, the subsequent deterioration and the final improvement were not mere accident, as the turn for the worse started the moment the insulin therapy was stopped.

If, however, there were really two different processes acting at the same time on the ocular apparatus in the chiasmal region, new problems would arise. In this connection some experiences of Zondek [37] and Feigenbaum [38] are worth noting. Zondek has drawn attention to a condition which he called "salt water obesity." The main symptom is chronic headaches, which according to his opinion are due to an increase of cranial pressure; he expressed the belief that the increase in pressure is caused by a retention of water and of salts in the cerebral tissue. The localization of this condition in the vicinity of the chiasma could be indicated by bitemporal hemianopic defects (Feigenbaum) which disappeared as well as by headaches after dehydration therapy and other measures aimed at removal of the salts. In one of Zondek's cases, in which the sella turcica was enlarged and there were genital symptoms in addition to headaches, the bitemporal hemianopia for colors also disappeared after such internal therapy. According to Zondek this fact showed "not only that the pressure of a growing tumor (probably a chromophobe adenoma) caused the changes in the field of vision but that processes responsive to therapy, in the vicinity of the tumor, were causative factors."

The cases of Zondek and Feigenbaum and the case I have reported are different in many aspects, but they seem to have one point in common, the indication that a pituitary disease may influence the optic pathways not only directly, by the pressure of an existing tumor, but also indirectly. If this observation could be confirmed by other cases it would be, I think, interesting from an ophthalmologic as well as from an endocrinologic standpoint.

In 1905 Schnabel [39] discussed the possibility of a nonmechanical influence upon the chiasma. In his case of a tumor of the pituitary gland with enlargement of the sella turcica, in the first one and one-half years there was alternating amaurosis of the right and of the left eye with temporal hemianopia of the eye not blind. At the end of this

37. Zondek, H.: Acta ophth. orient. **1**:88, 1939.

38. Feigenbaum, A.: Acta ophth. orient. **1**:28, 1938.

39. Schnabel: Ztschr. f. Augenh. **13**:70, 1905.

period the visual fields and the central vision were normal and the optic disk was pale at the temporal side. The improvement lasted one and one-half years. In the last period there was a paracentral scotoma and then temporal hemianopia on the right and later on the left. Schnabel stated the belief that the visual disturbances were not caused by pressure of the tumor and considered toxic influences on the crossed fibers of the optic nerve. His opinion was rejected by other authors and afterward not mentioned in the literature as far as I know. Probably Schnabel's

Visual Function in Cases of Lipaemia Retinalis Without Coma

Author	Age	Sex	Visual Function	Blood Fat, Gm. per 100 Cc.	Blood Sugar, Mg. per 100 Cc.
Heyl, 1880 (Heyl, A. G.: Philadelphia M. Times **10**: 318, 1880)	20	♂	Dim sight	.....	...
Reis, 1903	28	♂	20/200, 20/100; disk pale	18,129	...
Turney and Dudgeon, 1906	35	♀	Normal (rough tests)	12,811	...
Köllner, 1912	25	♂	Normal (rough tests)	.....	...
Darling, 1912	48	♂	R. 20/200, L. 20/30; decreased in last weeks	.....	...
Moore, 1915	23	♂	Normal	.....	...
Hardy, 1921	29	♂	R. 20/15, L. 20/38	9.5	278
McGuire, 1922	33	♂	Both eyes 20/20	8.6	540
Wagener, 1922	10	♀	Both eyes 6/5	3.5	400
McCann, 1923	15	♂	Both eyes 10/10	9.5	865
Rowe, 1923	15	♀	Blurred, hazy	>15	252
Machlis, 1924	24	♂	"Virtually amaurotic" after coma disappeared; later, normal	.....	...
Ferber and Appelman, 1927	38	♂	Blurred; normal after lipaemia retinalis disappeared	18.5	...
McKee and Rabinowitsch, 1931	14	♂	Both eyes 6/6	9.24	1,040
Chase, 1931	17	♂	Normal	10.57	370
Jaffe and Schonfeld, 1933	30	♂	No complaints	21.7	226
McKee, 1941	25	♂	Both eyes 6/6	....	...
Igersheimer	35	♂	Both eyes perception of hand movements; later, bitemporal hemianopia	6.8	392

theory was not correct. I am unable to offer an explanation for the course in his unusual case, which was of course different from that in the present case. I mention the discussion because of Schnabel's doubt that in his case pressure of the tumor was the (or the only) cause of the visual disturbances.

SUMMARY

The case here reported of acromegaly complicated by diabetes with retinal lipemia and peculiar visual disturbances seems to be the first published case of its kind. The condition behaved in many respects similarly to conditions observed experimentally (hyperglycemia, glycosuria, hyperlipemia, no particular loss of weight and a high resistance

to insulin). Analysis of the ocular changes makes it appear likely that two processes were going on in the pituitary-diencephalic region. One was characterized by bitemporal hemianopia and was caused by the pressure of a pituitary tumor. The other one is supposed to have been superimposed on the first, had involved the central vision and the visual field as a whole and was located probably in the diencephalic region. It is of ophthalmologic and of endocrinologic interest that these disturbances could be favorably influenced as well by insulin treatment as by roentgen ray treatment.

SEVERE UVEITIS WITH ASSOCIATED ALOPECIA, POLIOSIS, VITILIGO AND DEAFNESS

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Parker [1] in a de Schweinitz Lecture mentioned a patient whom I have seen. She was sent to me so that I might determine whether or not she was eligible for a state pension for blindness.

The clinical and laboratory findings are here recorded.

REPORT OF A CASE

A. T., aged 30, an Italian by birth, was the mother of eight children, seven of whom were living. The youngest was 1 year old and the oldest 13. The patient's father and mother were first cousins.

She was operated on in Hahnemann Hospital Nov. 10, 1938. The diagnosis was endometritis and acute salpingo-oophoritis on the left side.

On Feb. 10, 1939 she noticed on awakening in the morning that the vision of the right eye was very poor and that of the left eye somewhat impaired. There was headache, with a feeling of pressure in the eyes, more noticeable in the right eye. She was totally deaf.

On February 11 the patient was admitted to Wills Hospital to the service of Dr. Warren S. Reese. She was not acutely ill. In the right eye there was neuroretinitis. In the left eye the fundus was normal except for slight dilatation of the retinal veins. Four days later there was copious exudate about the disk, the retina was edematous and there was a detachment of the retina in the lower part of the fundus. On February 16 there was neuroretinitis in the left eye. The diagnosis was retrobulbar neuritis.

On February 11 vision in the right eye was counting of fingers at 18 inches (46 cm.), approximately 1/60; that in the left eye was 6/30. On February 13 vision was 1/60 in the right eye and 5/120 in the left. The upper eyelids drooped, the lashes were normal and the bulbar conjunctivas were injected. The eyeballs were tender to pressure, the hearing was good and hair and scalp were normal.

A complete physical and laboratory examination was made while the patient was in Wills Hospital. The main findings were chronic tonsillitis, chronic cervicitis and pyelitis on the left side.

On February 16 the patient was transferred to Jefferson Medical College Hospital. Laboratory examinations there gave the following results: urine, specific gravity 1.026 and albumin and sugar absent; blood, sugar content 91 mg. and urea nitrogen content 13 mg. per hundred cubic centimeters; Meinicke reaction, negative; Wassermann reaction, negative; cerebrospinal fluid, pressure 170

1. Parker, W. R.: Severe Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch. Ophth. **24**:439 (Sept.) 1940.

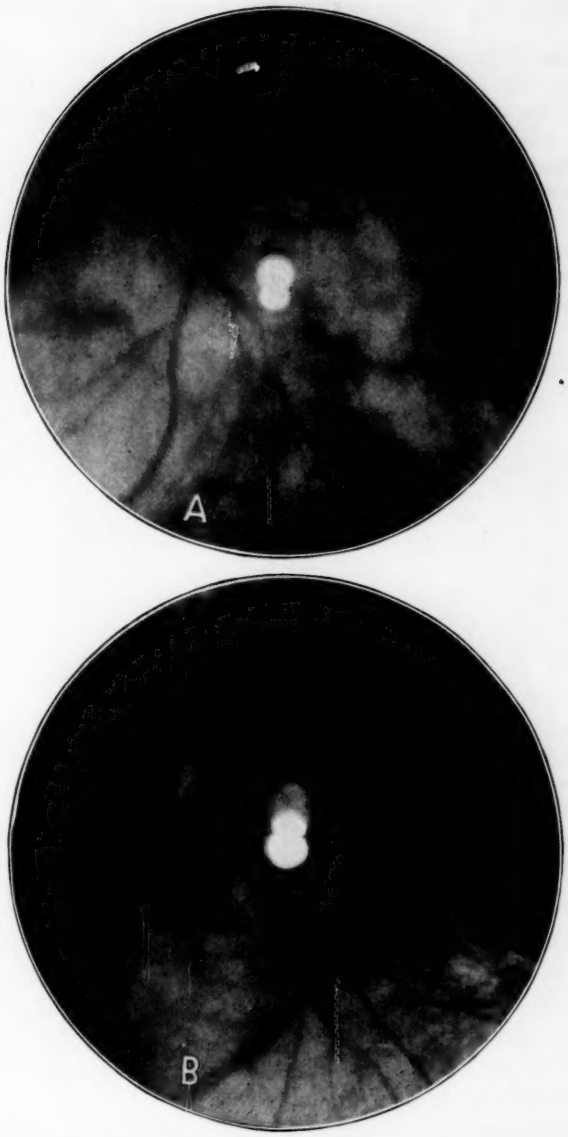

Fig. 1.—*A*, fundus of the right eye, showing extensive depigmentation of the choroid and the retina. *B*, fundus of the left eye, showing depigmentation of the epithelium of the retina and superficial atrophy of the choroid.

mm., cell count 602, reaction for globulin strongly positive, colloidal gold curve 00120000000 $\frac{C}{O}$ and culture negative. While no record could be found of a tuberculin test, the patient recalled that one had been made and had given negative results.

At the time of the patient's first visit to me, June 14, 1939, vision in each eye without glasses was 3/180. There was almost complete bilateral poliosis of both the supercilia and the cilia, and there was a patch of vitiligo in the superciliary region on the right side. The right pupil was oval, measuring 4.5 by 6 mm. The left pupil was round, measuring 7 mm. in diameter, and was slightly eccentric nasally. Both irises were inactive to light and in convergence. The upper lids drooped. The tension in each eye was 22 mm. of mercury (Schiøtz). The fields of vision showed concentric contraction almost to fixation, but the contraction was not so great for the left eye.

Ophthalmoscopic Examination.—On the anterior capsule of the right lens, surrounding the pupillary border from 3 to 11 o'clock, there was a line of equally spaced pigment dots, and at 7 o'clock there was a firm posterior synechia. There were dense opacities in the vitreous. The optic disk was dimly seen; it appeared very pale. The retinal vessels were diminished in size. Surrounding the disk there was a slightly elevated narrow zone of white exudate. There was partial atrophy of the choroid throughout the fundus. Broad bands of connective tissue stretched out over the retina; one such band on the nasal side of the disk was in advance of the retina. There was some free pigment in the periphery of the fundus, with no characteristic arrangement. The left eye showed a line of fine pigment on the anterior capsule of the lens close to the margin of the pupil extending from 8 to 4 o'clock, and at various other places on the capsule there were granules of pigment. The opacities in the vitreous were less dense than in the right eye. The fundus picture was similar to that of the right eye, but the vessels were of a better size. The areas of the choroid in which atrophy was most complete were lobulated.

Biomicroscopic Examination.—In addition to the changes observed with the ophthalmoscope, the right eye showed some deposits of pigment on the posterior surface of the cornea and on the anterior capsule of the lens. In the left eye there was fairly general distribution of fibrin over the posterior surface of the cornea and the anterior capsule of the lens, but there was no aqueous flare. It was difficult to follow the light beam into the lens.

The interesting features of the case are the consanguinity of the parents and the large area of choroidal atrophy. From the early clinical reports, as supplied by Dr. Warren S. Reese and Dr. C. E. G. Shannon, the case seems to have presented features somewhat similar to bilateral acute diffuse serous choroiditis (Harada's disease), as there were a bilateral diffuse exudate, neuroretinitis and detachment of the retina, with diffuse atrophy of the pigment layer.

As the literature was reviewed by Parker up to 1939, and as I have information that it is to be again thoroughly reviewed to date, I have contented myself with simply reporting the case history.

Dr. Walter I. Lillie provided the photographs of the external and of the fundus lesions. Because of the condition of the media it was impossible to get sharp details of the fundus.

Fig. 2.—The patient, showing poliosis of the eyelashes and eyebrows and vitiligo in the superciliary region.

UNIV. OF MICH.

LESIONS IN THE LENS CAUSED BY PURULENT CORNEAL ULCERS

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Before the invention of the ophthalmoscope, the teaching of ophthalmology was of three main types, namely, the teaching of ophthalmia, the teaching of cataract and the teaching of blindness. Of these three, the teaching of cataract was the best developed, owing largely to its frequency and to the good results obtained by removing cataracts. At first the most obvious facts concerning cataracts were observed. Details were learned subsequently. In recent years the employment of the slit lamp has aided enormously in revealing lesions in the living lens and in observing their progress or arrest. In the field of experiment, epithelial cells from the lens have been cultivated and studied in various relations. The surgery of the lens has not lagged behind. With a refinement of technic gradually evolved, the method of intracapsular extraction has become a standard one.

An understanding of the pathology of the lens is essential in order to complete the knowledge gained from surgical experience. Certainly every intracapsulary extracted lens should be sent to the laboratory for study, as is the rule with other surgically removed tissues of the body. An example of the clinical value of a pathologic examination of lenses is a report by Reese [1] on a series of cases of radiation cataract. He demonstrated that this form of cataract is characterized by a proliferation of the subcapsular epithelium, and he gave it as his opinion that this proliferation will continue unless the entire capsule is removed; hence the merit of the intracapsular operation in the removal of radiation cataract.

The present paper is concerned with alterations in the lens brought about by bacterial toxins diffused from corneal ulcers across the anterior chamber space. Forty globes were studied, in each of which there was a more or less active purulent ulcer at the time of enucleation.

Read at the Seventy-Seventh Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 5, 1941.

1. Reese, A. B.: The Operative Treatment of Radiation Cataract, Tr. Am. Acad. Ophth. **43**:177, 1938.

GENERAL FEATURES

1. *Necrosis of Subcapsular Epithelium.*—Attention was called in the preparations to a relation between damage to the subcapsular epithelium and damage to the endothelium lining Descemet's membrane. Necrosis of the one was almost always accompanied by necrosis of the other. In several cases the necrotic endothelium was cast off in plaques and at the same time the necrotic subcapsular epithelium had entirely disappeared or had collected in small pyknotic masses. There were instances in which the endothelial and epithelial necrosis was accompanied with necrosis of the iris as well as of the ciliary processes, thus emphasizing the far reaching effects of a distant ulcer and accounting for the prolonged period of severe inflammation that follows in its trail. According to von Hippel the disappearance of the subcapsular epithelium may serve a good purpose, since it permits the aqueous to permeate through the capsule and in this way aids in liquefaction and absorption of degenerated lens matter.

2. *Proliferation of the Subcapsular Epithelium.*—In the milder ulcers the subcapsular epithelium merely underwent protoplasmic alterations, a disturbance in order or a primary proliferation. A double row of cells frequently appeared, and probably there would have been more cells later had not the eye been removed within a short period after the onset of the ulcer. It was believed that the changes found depended primarily on the toxicity of the bacteria and on the power of the structures to react. There were 2 instances, one of ophthalmia neonatorum and the other of keratomalacia, in each of which an eye of an infant under 3 weeks of age was involved, in which a relatively small difference was noted in the subcapsular epithelium, probably because the germs lacked sufficient virulence. This finding agrees with clinical experience that occasionally a small serpiginous ulcer will give rise to a large hypopyon, whereas a large ulcer may give rise to a little hypopyon or to none.

3. *Area of Subcapsular Epithelium Involved.*—The most pronounced alterations in the subcapsular epithelium occurred in the pupillary area, where the lens is not covered or protected by the iris but where it is directly exposed to toxins diffused from the cornea. This held true whether or not the ulcer was in the central area of the cornea or off to one side. Generally when the epithelial cells multiplied, as in the milder ulcers, the process was well within the pupillary area. On the other hand, when necrosis of the epithelium took place, as in the more severe ulcers, it usually extended over a wider area. Probably in the milder ulcers the first effect of the toxins was to cause a contraction of the pupil by irritation, which left a small exposure. In the virulent ulcers it may have been that the moment the concentrated toxins reached the iris they paralyzed the sphincter and prevented it from contracting. As a sequel

of a serpiginous ulcer the iris may rapidly shrink into the angle of the anterior chamber and become almost invisible.[2]

4. *Complicating Causative Factors.*—Many of the globes exhibited signs of disease that had probably affected the lens before the onset of the ulcer, which only sealed the fate of the organ. Glaucoma, thrombosis of the central vein of the retina, diabetes and old age were mentioned in the histories. Their destructive action on the subcapsular epithelium and the lens substance is well established; it is caused by disorder or deficiency of nutrition. A differentiation between recent changes caused by the bacterial toxins and by antecedent senile or glaucomatous changes was sometimes difficult to make. In the 12 cases of perforation, in several of which the iris or the lens had prolapsed, it was usually easy to decide which alterations antedated the perforation, because perforation led to almost immediate enucleation, especially in blind glaucomatous eyes.

DETAILS OF CHANGES WITHIN THE LENS

1. *Pus Cells in the Lens.*—In this large series of globes with purulent ulcers, so many of which had produced hypopyon, there was but 1 in which there were pus cells within the lens capsule. This was from a patient with herpes iridis in whom a perforating ulcer had caused an iridocyclitis that filled the anterior and the posterior chamber with pus (fig. 1 *A*). No defect was found in the capsule, which was not wrinkled, as it is when lens matter is extruded. However, the possibility of a defect at some point in the thin posterior capsule, which was surrounded by pus cells, could not be excluded, since serial sections were not available. Anteriorly a layer of leukocytes lay between the subcapsular epithelium and the cortical fibers. The point was that whereas the epithelium was in disorder, with here and there a necrotic cell, the subjacent cortical layers were unaltered. In spite of failure to find a defect in the capsule, my belief in the active impermeability of the lens capsule to cells remains unshaken.

2. *Liquefaction Necrosis of Lens Fibers.*—It had been my impression that the subcapsular epithelial cells are more sensitive to all forms of injury than the subjacent lens fibers. If this is the rule, one specimen seemed to be an exception to it. This was from a woman 49 years old. For some time the eye had been blind from glaucoma. The epithelium was in order and without recognizable change, and yet beneath it there spread out a stratum of liquefied lens fibers (fig. 1 *B*).

3. *Proliferation of the Subcapsular Epithelium.*—The epithelial cells are the only tissue in the lens capable of growing, of responding to

2. Samuels, B.: Necrosis of the Iris, Tr. Ophth. Soc. U. Kingdom **49**:421, 1928.

stimuli and of reproducing themselves, which properties are commonly associated with life. Therefore, much of the attention in this study centered in the responses of the subcapsular epithelium to bacterial toxins.

(*a*) Example of Rapid Proliferation: A severe ulcer in the cornea of a youth 17 years of age followed an attack of dacryocystitis. The eye was enucleated three weeks after the onset. The lens lay in contact with a purulent cornea and a mass of exudate that filled a large central defect (fig. 2 *A*). Situated underneath the exudate were two anterior polar cataracts, a most unusual finding, since there is usually only one.

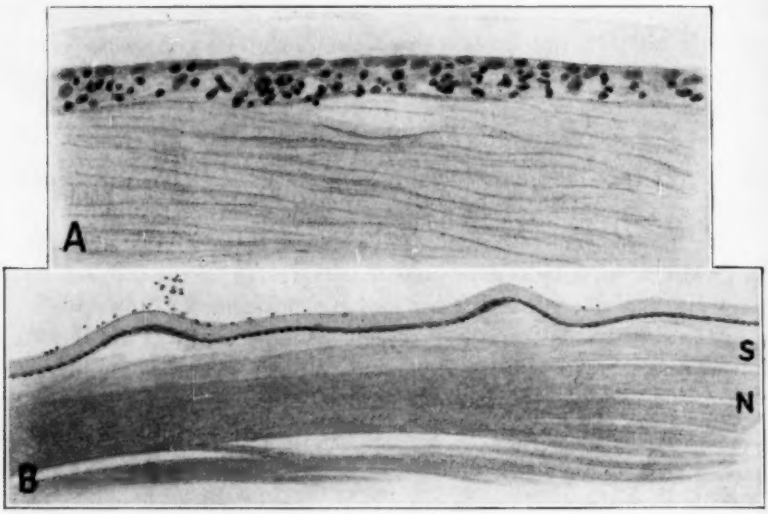

Fig. 1.—*A*, herpes iridis; migration of pus cells forward after probable erosion of a thin posterior capsule. The picture shows pus cells near the anterior pole of the lens, where they lie between capsular epithelium and cortical substance. Here and there an epithelial cell has fallen back among the pus cells. The great amount of cellular debris indicates that many of the leukocytes underwent necrosis. The cortical layers are not affected. *B*, folding of the lens capsule and liquefaction of the cortex. The detail is from a blind glaucomatous eye of a woman aged 49. Two weeks before enucleation a serpiginous ulcer developed. The liquefaction of the subcortical layers (*S*) was supposed to be caused by toxins elaborated by bacteria in the distant cornea. At *N* is the intact nucleus. The anterior capsular epithelium is normal.

They were separated from each other by a stretch of almost normal epithelium. The dual cataracts had developed with incredible speed.

An informative detail was the wrinkling of the capsule over the larger cataract, manifesting an early and inherent property of the proliferated cells to contract (fig. 2 *B* and *C*). Another notable feature

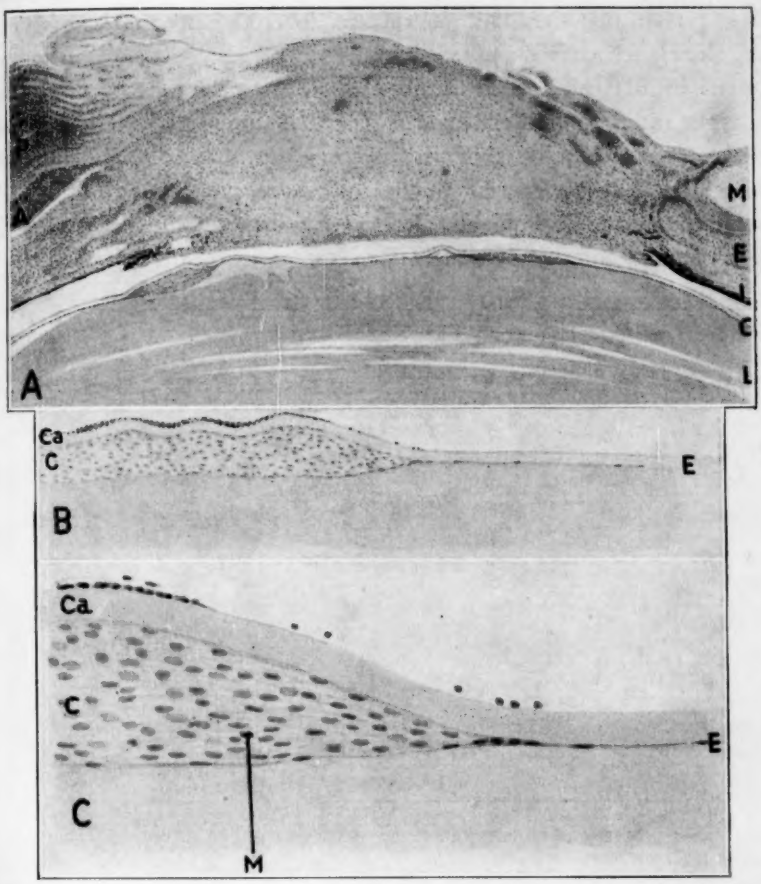

Fig. 2.—*A*, serpiginous ulcer in a youth 17 years of age; early formation of an anterior capsular cataract. At *P* there is a dense purulent infiltration of the cornea and at *A* a part of a posterior abscess. To the right the margin of the perforation (*M*) is separated by exudate (*E*) from the iris (*I*). Necrotic pus and blood occupy the central defect of the cornea. The capsule of the lens (*C*) is thrown into folds in two places, each enclosing a clear fluid. In connection with the folds there are two plaques of newly proliferated capsular epithelium (anterior polar cataract). The larger one clings to a fold of the capsule and is partly lifted above the cortex. Elsewhere this fold passes over an area of liquefied lens substance that extends deep into the cortex. *B* and *C*, details of *A*. To the left of drawing *B* is shown the larger cataract, composed of recently proliferated capsular epithelium (*C*), which detaches the capsule (*Ca*). The cells are oblong, regular and rich in protoplasm. In drawing *C* as an expression of rapid proliferation *M* points to a typical mitotic figure. The epithelial layer (*E*) adjoining the proliferation is exceedingly flat and rarefied. It extends under the cataract, sealing it off from the underlying liquefied cortex.

was the behavior of the epithelial cells that bordered the outer margins of each cataract. They were sparingly disposed and exceedingly flat. It was certain that they had not replaced necrotic subcapsular epithelial cells, since such cells do not disappear so quickly and are not at once replaced by flat cells. This rarefied single layer of cells grew beneath the larger cataract and delineated it from the subjacent liquefied cortical substance. It may be that the protoplasm of the peripheral cells assumed a flat shape in order to enable them to creep along the capsule. It would not be strange if the epithelial cells of the lens, like those elsewhere, should evince a tendency to move toward places (positive

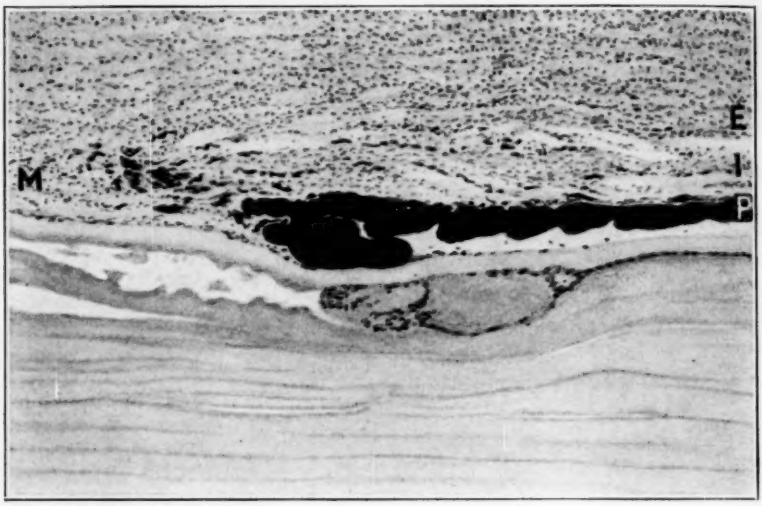

Fig. 3.—Proliferation of lens substance at the margin of an area of necrosis in the capsular epithelium. The eye was removed six weeks after a lime burn of the cornea which became complicated by a serpiginous ulcer. Purulent exudate filled the anterior chamber. There is an accumulation of pigment (*P*) at the pupillary border. The stroma of the iris (*I*) blends with the overlying organized exudate (*E*), which forms a membrane (*M*) over the pupillary area. Under this the capsular epithelium is completely absent (necrosis) and the cortical layers are destroyed. To the right, under the pupillary area of the iris, the epithelium is well preserved. At this margin of the necrotic field the epithelium has proliferated and laid down several nodules of a homogeneous substance.

chemotaxis) or away from places (negative chemotaxis), the direction being determined by substances which exert a chemical influence.

(*b*) Formation of New Lens Substance: In contrast to the case mentioned of proliferation of the central subcapsular epithelial cells, there was a case in which the opposite process occurred. The central subcapsular epithelium was entirely missing because of necrosis (fig. 3).

Surrounding the denuded area, the epithelial cells halted, proliferated and secreted a clear substance that formed a ring about the necrotic field, reminding one of Soemmerring's crystalline ring, which develops after the removal of a lens nucleus. In thus laying down lens substance in the presence of an emergency, the subcapsular epithelium, whose special function is a nutritive one, exhibited a physiologic capacity that one would not have attributed to it.

CONCERNING THE TOXICITY OF THE CONTENTS OF THE ANTERIOR CHAMBER

The question arose as to how much of the toxins of a corneal ulcer is diffused into the conjunctival sac, where they are harmless, and how much is diffused into the anterior chamber, where they are harmful. It was notable that in some cases the advancing border of an ulcer lay under a heavy coating of corneal lamellas, so that it had the aspect of an abscess. In other cases the advancing border was partly exposed to the free surface of the ulcer. The theory was that in an ulcer of the abscess type less of the toxins than in the open type is diffused into the conjunctival sac and just so much more is left to be diffused into the anterior chamber. In agreement with this observation, hypopyon became associated with "closed ulcers" and clear aqueous with "open ulcers." It was recognized that the most toxic and destructive form is ulcer serpens with a typical posterior abscess.[3]

The state of the angle of the anterior chamber was surveyed. For those cases in which there were glaucomatous changes, in which the angle was blocked, the term "closed empyema" of the anterior chamber was used, and for those cases in which the angle was patulous, the term "open empyema" was used, in the sense that one speaks of an open or a closed empyema of the accessory sinuses. It was reasoned that the contents in a closed chamber would be more concentrated and toxic than those in an open chamber. It was borne in mind that in hypopyon ulcer the bacterial toxins in the anterior chamber, which are of exogenous origin, while they may be the chief ones, are not the only ones to be found. There develop endogenous toxins, particularly from autolysis of the leukocytes which compose the exudate. Desquamated and necrotic endothelial cells from the lining of the anterior chamber add their proportional share. In the present series disintegrating red blood cells were seen occasionally in the exudate, forming an association of hyphemia and hypopyon. The toxic effect of decaying erythrocytes is well known. Another source of endogenous toxins is the stroma of the iris when it becomes necrotic.

3. Samuels, B.: Methods of Formation of the Posterior Abscess in Ulcus Serpens, Arch. Ophth. **7**:31 (Jan.) 1932.

EFFECTS OF HYPOPYON ON THE LENS

In conclusion, the study led to the belief that a hypopyon, particularly one rich in fibrin, in its early stages protects the lens from bacterial toxins and that later, as it decomposes, it is actually harmful to the iris and the lens. In a given case it was never possible to decide how many of the alterations in the lens had taken place before the advent of the hypopyon. It was proved by a number of cases that bacterial toxins from the cornea can produce changes in the lens in the absence of hypopyon.

CHARACTERISTICS OF THE AVERAGE NORMAL NERVE HEAD

WITH REFERENCE TO CLASSIFICATION OF OPTIC NERVE ATROPHY

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The differential diagnosis between primary and postneuritic optic nerve atrophy is sometimes decided by one or two minute anatomic details. Attention is paid chiefly to the presence of the physiologic cup, to the visibility of stippling of the lamina cribrosa, to the absence of connective tissue on the disk or vessels, to the integrity of the disk outlines and to the regular distribution of pigment around the nerve. If deviations from the normal under these headings are noted they are presumptive evidence that an inflammation of the nerve has antedated its atrophic state.

But how much right on the basis of statistical inquiry does one have in assuming that the nerve should possess a well defined cup or a visible lamina cribrosa, that the borders of the disk should be sharp, without adjacent pigmentary derangement, or that connective tissue should be absent?

If only one nerve is atrophic a comparison may be made with the healthy eye. Supposing the normal eye to be typical in appearance, is one justified in assuming that the affected nerve had possessed similar characteristics before the onset of disease? How often are the normal markings found bilaterally?

In order to provide an answer to these questions I recorded the appearance of the optic disks in 312 consecutive patients, or in 624 eyes. The continuity of the series was broken only to eliminate patients with diseased eyes and patients in whom both nerves could not be examined clearly.

It is recognized that a survey of this kind might yield figures which would vary according to the interpretations of individual observers. Table 1 summarizes the findings.

Only 220 nerve heads (35.2 per cent) presented the classic "normal" appearance; 404 (64.7 per cent) were stigmatized by failure to possess one or more of the "normal" characteristics.

When the normal markings of the lamina cribrosa were present on both sides but were more accentuated on one side and when cupping

was present on both sides but more marked on one side, cognizance was taken that bilateral comparison would be untrustworthy. If patients in whom such situations existed are included (30 patients, or 9.6 per cent) the percentage for whom differential diagnosis would be difficult tends to rise.

TABLE 1.—*Summary of Examination of 624 Eyes* *

	Number of Patients	Percentage of Patients
Stippling of lamina cribrosa		
Present on both sides	109	35
Absent on both sides	168	54
Present on one side (absent on other)	35	11
Absent in 371, or 60%, of the eyes		
Cupping		
Present on both sides	192	62
Absent on both sides	92	30
Present on one side (absent on other)	28	8
Absent in 212, or 34%, of the eyes		
	Number of Eyes	Percentage of Eyes
Blurring of margins		
In both eyes	18 (9 patients)	2.9
In one eye	16 (16 patients)	2.5
	34	5.4
Abnormal pigmentation		
Around both nerves	14 (7 patients)	2.3
Around one nerve	11 (11 patients)	1.7
	25	4.0
Presence of connective tissue		
On both disks	30 (15 patients)	4.8
On one disk	24 (24 patients)	3.8
	54	8.6
	Number of Patients	Percentage of Patients
Absence of bilaterality of normal markings	114	36

* The age of the patient bore no relation to the appearance of the disk.

TABLE 2.—*Presence of "Confusion Signs"*

Number of Signs Present	Number of Eyes	Percentage of Eyes
1	151	24.2
2	189	30.5
3	53	8.4
4	10	1.6
5	1	...
	404	64.7

The coexistence of two or more "confusion signs" reduces the total statistical percentage of eyes for which diagnosis is rendered difficult, but it increases the difficulty of interpreting the nerve picture of the particular eye involved. If a diagnosis of postneuritic atrophy were based on the absence of cupping or of stippling of the lamina cribrosa, on blurring of the disk margins, on abnormal peripapillary pigmentation or on the presence of connective tissue on the disk or the vessels, about two thirds

of normal eyes would mislead the examiner. Table 2 shows the number of times these signs were present in combination.

There were only 15 eyes in which the markings of the lamina cribrosa were evident in the presence of other "confusion signs." Thus the presence of stippling of the lamina cribrosa seems to be insurance against abnormal signs in the great majority of cases.

Stippling of the lamina cribrosa was present and cupping absent in 6 eyes, or 2.8 per cent, of 212 eyes in which no cupping existed. Stippling of the lamina cribrosa was absent and cupping present in 159 eyes, or 38 per cent, of 412 eyes in which cupping was present.

Temporal pallor of the disk in intensity bordering on the abnormal was found in a number of cases (23 eyes, or 3.6 per cent), but these were not included in the tabulations.

TABLE 3.—*Relation of Cupping and of Visibility of the Lamina Cribrosa to Refractive Errors*

		No.	%		No.	%
Hyperopic eyes..... 317	Cupping present	215	67	Lamina cribrosa visible	140	44
	Cupping absent	102	33	Lamina cribrosa absent	177	56
Myopic eyes..... 215	Cupping present	126	58	Lamina cribrosa visible	70	32
	Cupping absent	89	42	Lamina cribrosa absent	145	68
Emmetropic eyes.. 68	Cupping present	57	83	Lamina cribrosa visible	37	54
	Cupping absent	11	17	Lamina cribrosa absent	31	46
Mixed astigmatism 24	Cupping present	14	58	Lamina cribrosa visible	6	25
	Cupping absent	10	42	Lamina cribrosa absent	18	75

Out of curiosity I tabulated the relation of cupping and of the visibility of the lamina cribrosa to the refractive errors. The results are shown in table 3.

COMMENT AND CONCLUSIONS

In the interpretation of this series of examinations the following question was always kept in mind: If the nerve under examination should become the victim of primary atrophy, would the markings lead to an unjustified diagnosis of postneuritic atrophy?

Two thirds of the average normal optic nerves possessed characteristics which might under certain conditions be interpreted as postinflammatory. Only one third of the nerve heads examined possessed the classic "normal" appearance.

In nearly 10 per cent of the patients the two nerves showed sufficient inequality of cupping and sufficient differences in visibility of stippling of the lamina cribrosa to mislead the observer toward an unjustified

impression of previous neuritis in the less typical eye if optic nerve atrophy should be present.

Slightly more than one third of the patients presented unilateral absence of cupping, absence of stippling of the lamina cribrosa or other atypical markings of the disk. An erroneous diagnosis of postneuritic atrophy might be made if the atypical nerve were to become atrophic.

When all the diagnostic points are taken into consideration, two thirds of the eyes examined might have offered some difficulty in ruling out previous neuritis had primary optic nerve atrophy been found.

ANISEIKONIA

A REFINEMENT OF REFRACTION

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The introduction of aniseikonic lenses has not changed the cardinal points of refraction. The chief aim of the refractionist is still to relieve asthenopia and to prescribe glasses as seldom as possible.

Much of the fundamental knowledge about aniseikonia has been known but unused for many years.[1] Out of recent studies has come a method of measuring and correcting errors in the size and shape of the ocular images so sensitive that existing errors may be corrected to the limits of observation. The latest method (with the American Optical eikonometer) is simple and rapid in most cases, and the aniseikonic glasses do not differ greatly in appearance from ordinary power lenses.

The average person with 20/20 vision is able to recognize repeatedly differences of 0.25 per cent in the size of the ocular images, while the astute observer may note differences of 0.10 per cent.[2]

Few clinicians care to wade through the physiologic optics [3] that forms the basis for a consideration of the importance of differences in size of the ocular images, or aniseikonia. Without such a background,

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1. Berens, C., and Loutfallah, M.: Aniseikonia: Study of Eight Hundred and Thirty-Six Patients Examined with Ophthalmo-Eikonometer, Am. J. Ophth. **22**:625-641 (June) 1939.

2. Gliddon, G. H.: Aniseikonia, J. Optic. Soc. America **30**:142-144 (April) 1940.

3. (*a*) Ames, A., Jr., and Proctor, C. A.: Dioptrics of the Eye, J. Optic. Soc. America **5**:22-84 (Jan.) 1921; (*b*) Aberrations of the Eye, Am. J. Physiol. Optics **4**:3-37, 1923. (*c*) Ames, A., Jr.: Cyclophoria, ibid. **7**:3-38, 1926. (*d*) Ames, A., Jr., and Gliddon, G. H.: Ocular Measurements, Tr. Sect. Ophth., A. M. A., 1928, pp. 1-68. (*e*) Gliddon, G. H.: Optical Replica of the Human Eye for Study of Retinal Image, Arch. Ophth. **2**:138-163 (Aug.) 1929. (*f*) Ames, A., Jr.; Gliddon, G. H., and Ogle, K. N.: Size and Shape of Ocular Images: I. Methods of Determination and Physiologic Significance, ibid. **7**:576-597 (April) 1932. (*g*) Carleton, E. H., and Madigan, L. F.: Size and Shape of Ocular Images: II. Clinical Significance, ibid. **7**:720-738 (May) 1932. (*h*) Ames, A., Jr., and Ogle, K. N.: Size and Shape of Ocular Images: III. Visual Sensitivity to Differences in the Relative Size of the Ocular Images of the Two Eyes, ibid. **7**:904-924 (June) 1932; (*i*) The Horopter and Corresponding Retinal Points, Ann. Distinguished Serv. Found. Optom. **1**:35-45, 1932. (*j*) Ames, A., Jr.;

(Footnote continued on next page)

evaluation of the place of aniseikonic measurement and correction is difficult, and the results are apt to be false.[3s]

Aniseikonia is a binocular function. Most refractions unfortunately are still done as monocular examinations. More attention to binocular functions will make for more refined refractions. It has been shown that usually when the ocular images of the two eyes vary in size more than 5 per cent binocular vision is no longer possible because of the difference in the spatial localization of the two objects.[3n]

There are at present four known causes of aniseikonia. The ocular images may vary in size (1) on a physiologic basis, e. g. differences in the spacing of the rods and the cones [3m]; (2) on the psychologic basis [4]; (3) because the object fixated is at a different distance from each eye,[5] or (4) on the basis of different magnification effects of the prescribed lenses.[6] It is important to understand the magnification effects of a dioptric lens, which depend on its surface curves, its thickness, and its position in front of the eye. In general the magnification properties of any lens are the product of its shape magnification and power magnification in its principal meridians. Prisms have an asymmetric magnification effect. Thus, ordinary dioptric lenses may add to or subtract from the aniseikonia inherent in any patient. Any measurement of

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Gliddon, G. H., and Ogle, K. N.: The Importance of the Relative Size and Shape of Ocular Images in Vision, ibid. **1**:46-60, 1932; (*k*) Lenses for Changing the Size and Shape of Dioptric Images, ibid. **1**:67-70, 1932. (*l*) Madigan, L. F., and Carleton, E. H.: A Clinical Report of Corrections of Differences in Size and Shape of Retinal Images, ibid. **1**:71-92, 1932. (*m*) Erggelet, H.: Anisometropie: methodisch-experimentelle Betrachtungen, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **49**:326-361, 1915-1916. (*n*) Ogle, K. N.: The Correction of Aniseikonia with Ophthalmic Lenses, J. Optic. Soc. America **26**:323-337 (Aug.) 1936; (*o*) Relative Sizes of Ocular Images in Asymmetric Convergence, Arch. Ophth. **22**:1046-1067 (Dec.) 1939; (*p*) Induced Size Effect in Asymmetric Convergence, ibid. **23**:1023-1038 (May) 1940. (*q*) Herzau, W., and Ogle, K. N.: Ueber den Grössenunterschied der Bilder beider Augen bei assymmetrischer Konvergenz und seine Bedeutung für das zweiäugige Sehen, Arch. f. Ophth. **137**:327-363, 1937. (*r*) Schubert, G.: Zur "Aniseikonia"-Frage, Arch. f. Ophth. **140**:55-60, 1939. (*s*) One of the best summaries of the subject is given by Ames, A., Jr.; Lancaster, W. B.; Bielschowsky, A.; Berens, C.; Hardy, W. F.; Barkan, O., and Jackson, E., in discussion on Jackson, E.: Importance of Aniseikonia, Tr. Sect. Ophth., A. M. A., 1936, pp. 27-48 (especially p. 40).

4. Ogle, K. N.: Induced Size Effect, Arch. Ophth. **21**:604-625 (April) 1939. Jackson, E.: The Importance of Aniseikonia, Am. J. Ophth. **20**:16-20 (Jan.) 1937.

5. Ludvigh, E. J.: Aniseikonia, Am. J. Ophth. **19**:292-301 (April) 1936. Ogle.[3o] Herzau and Ogle.[3q]

6. Carleton, E. H., and Madigan, L. F.: Relation Between Aniseikonia and Ametropia, Arch. Ophth. **18**:237-247 (Aug.) 1937.

aniseikonia must assume a constant refractive correction, accommodative state and heterophoric correction.

Roughly, each diopter of plus power in a lens is equivalent to 2 per cent magnification and each diopter of minus power to 2 per cent minification. Anisometropia therefore is closely related to aniseikonia, but there is no fixed relation between them because of the unknown factor, namely the aniseikonia, which exists prior to the refractive dioptric, or power, correction. Aniseikonic measurement frequently discloses the opposite condition from what would be expected on the basis of an estimation of the relative size of the images from the magnification effects of the power lenses alone.[6] Added comfort with anisometropic refractive corrections is to be expected from the correction of the aniseikonia in those patients who experience difficulty in wearing their anisometropic lenses. Aniseikonia should not be considered as the answer in full to all the problems of anisometropia. The prescribing of comfortable glasses is still an art, but a knowledge of the fine points in refraction requires consideration of the question of aniseikonia. Many refractive problems seem to have a close relation to the question of aniseikonia. Certain types of cyclophoria have been shown to respond satisfactorily to a meridional aniseikonic lens. The knowledge of aniseikonia has aided in the handing of many refractive problems by revealing a condition which may itself be the cause of asthenopia or may be combined with other refractive abnormalities as an added complication.

The question of compensation for existing aniseikonia has been raised by several authors,[7] and evidence has been produced,[3o] although it is not fully understood as yet, that there is such a compensation. Lancaster [8] compared it to the range of accommodation, or the range of fusion. In several cases "horror fusionis" has responded to difficult but carefully worked out aniseikonic corrections. That binocular vision and fusion are closely related to aniseikonia seems evident from the fact that 5 per cent differences in size between the images of the two eyes are sufficient to break the fusion faculty.

Whatever symptoms arise from aniseikonia depend on the erroneous spatial perceptions caused by differences in the size of the ocular images. These altered spatial perceptions are definite effects of the changed sizes of the ocular images, and they can be demonstrated simply by the putting on of a size lens. These changes can be measured

7. Discussion on Jackson.[3s] Herzau and Ogle.[3q] Ludvigh.[5]

8. Lancaster, W. B.: Aniseikonia, Arch. Ophth. **20**:907-912 (Dec.) 1938.

in several ways whether they exist primarily or are produced arbitrarily by the wearing of a size lens.

The measurable effects on spatial perception are measured with the assistance of the "tipping field," [9] the "leaf room," the S curve [4] and the eikonometer, which are all simple means of illustrating the changes in the horopter produced by changes in the size of the retinal or of the ocular images. Clinically, measurement of the images by means of the eikonometer is all that is required for calculation of the necessary correction for aniseikonia.

All investigators who have had experience in correcting differences in size have reported favorably, as shown in the accompanying table. There have been some remarkable cures, which have been inter-

Results of Aniseikonic Corrections

Author	Percentage of Patients Relieved of Symptoms	Number of Patients	Year of Publication
Carleton and Madigan [6]	57	829 500 followed	1937
Berens and Loutfallah [1]	73 74	711 125	1938
Hughes, W. L.: Am. J. Ophth. **18**: 607, 1935; **19**: 686, 1936; **20**: 887, 1937; Arch. Ophth. **17**: 944 (May) 1937	76-80 75.5 71	11 357 14 with emmetropia	1935 1936 1937
Berens, C.: Brit. J. Ophth. **21**: 132, 1937...	68.7	160	1937
Hardy, G.: Am. J. Ophth. **20**: 599, 1937....	41	34	1937
Doane, H. C.: Tr. Am. Acad. Optom. **8**: 117, 1933	66	35	1933
Doane, H. C.: Tr. Am. Acad. Optom. **9**: 179, 1935	72, definite 28, partial	94	1935

preted by the laity as miracles. With any new procedure there are times when its importance is overemphasized and others when it is sadly neglected. Because of the complicated interrelation between aniseikonia and the entire refractive setup, it is hard to judge the importance of the former. It is difficult to get accurate figures on the number of headaches relieved by the use of any type of glasses without trying to find out how many cures result from the use of cylinders, prisms or any other single unit of the refractive armamentarium.

Let the measurement of aniseikonia be added to the refractive procedure, and until the means for it is available to every refractionist, let the patient who has difficulty be given a chance to respond to correction with size lenses.

9. Ames, A., Jr.: Aniseikonia—A Factor in the Functioning of Vision, Am. J. Ophth. **18**:1014-1019 (Nov.) 1935.

HYSTERICAL CONVERGENCE SPASM

BENJAMIN F. SOUDERS, M.D.
PHILADELPHIA

Among the varied manifestations of hysteria it is not infrequent to find ocular disturbances which dominate or contribute to the symptom complex. The most common expressions of disturbances of this nature are visual. Extremes of visual abnormality are encountered, varying from slightly diminished visual acuity to amaurosis, and monocular diplopia or even polyopia is an occasional symptom. Objective disturbances of vision, as shown by the visual fields, can also frequently be found. These include tubular fields of vision, spiral fields of vision and reversal of color fields.

Ocular manifestations of hysteria are not limited to photosensory disturbances but occasionally are manifested by neuromuscular excesses or weaknesses of the eye and its adnexa. Thus, blepharospasm is an occasional occurrence of functional origin. Spasm and paralysis of the ciliary muscle and hippus were stated by Shastid [1] to occur as the result of hysteria. Bielschowsky [2] looked critically on spasms and palsies of extraocular muscles attributable to hysteria. He doubted the reliability of observations reported as purely hysterical paralysis, but he recognized a type of nonspastic ptosis with a hysterical basis as well as hysterical conjugate deviations, nystagmus, paralyses of associated ocular movements and convergence spasm.

Convergence spasm is perhaps one of the most clearly defined ocular motor anomalies which may occur as the result of hysteria. Cords [3] stated that the condition is a common disturbance of ocular muscle function which accompanies traumatic neurosis and hysteria. Its incidence cannot be estimated, but it must be considered unusual, judging by the infrequency of published case reports.

The diagnosis of convergence spasm is suggested when a patient presents abnormal and variable degrees of convergence. In some instances the condition is observed only when the patient looks at a

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1. Shastid, T. H.: Hysteropia, or the Ocular Manifestations of Hysteria, Am. J. Physiol. Optics **2**:289, 1921.

2. Bielschowsky, A.: Lectures on Motor Anomalies: XII. Ocular Spasms, Am. J. Ophth. **22**:856, 1939.

3. Cords, R., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 3, p. 617.

near object, but in others it is a constant finding. It is particularly noted when the patient is instructed to look at a specific object, such as a test letter. Intense miosis usually accompanies spasm of convergence, and it is this fact which will aid in differentiating the condition from concomitant convergent squint. Miosis is the accompaniment of an excessive accommodation-convergence act. The fact that accommodation is increased can be determined by retinoscopic examination of the patient before and after atropinization. Eight or 10 D. of excessive accommodation can sometimes be discovered in this manner.

Small difficulty is met in differentiating functional convergence spasm from paralytic heterotropia. Paresis of the external rectus muscle, however, may be confused with the condition, and when it is, the taking of diplopia fields and fields of rotation and careful observation of the ocular rotations will serve to establish a correct diagnosis. Bielschowsky [2] has emphasized the fact that an obscure paralytic type of heterotropia may be the background for a disturbance which appears to be a hysterical ocular anomaly. He has recounted a case in which unilateral blepharospasm resulted from the attempt to avoid diplopia by blotting out one image and another in which excessive convergence achieved the same end by shifting one image to the periphery of the binocular field of vision. The importance of ruling out isolated muscular pareses as the basis for ocular spasm is obvious. The diagnosis of convergence spasm demands that organic disturbances receive prime consideration until exhaustive examination and prolonged observation fail to disclose adequate cause for the symptom.

The mechanism of hysterical convergence spasm is of course obscure. The assertions of Babinski with regard to hysteria in general have been reaffirmed by Pfingst [4] in a discussion of the explanation of ocular hysteria. Babinski proposed that suggestion is the chief cause of hysteria: The disease is a pathologic state manifested by disorders which it is possible to reproduce exactly by suggestion in certain subjects.

Many normal persons are able to induce excessive convergence without the stimulus of a corresponding near point of regard. Homonymous diplopia is produced in which two blurred images can be placed at various distances apart depending on the degree of convergence. This is similar to the physiologic diplopia which one can produce by fixing a near object while regarding the blurred double images of a more distant object. The demonstration of these facts to a susceptible person of neuropsychiatric tendencies might well be the groundwork on which a hysterical symptom complex could be built. In this regard it seems justifiable to suppose that persistent or indiscriminate use of

4. Pfingst, A. O.: Hysteria as It Affects the Eye, Kentucky M. J. **18**:436, 1920.

muscle training exercises in certain cases might help to make hysterical convergence spasm more prevalent than it appears to be at present. Certainly the element of suggestion is present in many orthoptic training exercises commonly employed.

The treatment of functional convergence spasm is generally unsatisfactory unless the underlying cause for the neurosis can be uncovered. For this purpose psychiatric aid should be consulted, and Babinski's second aphorism, that persuasion or countersuggestion alone can be effective, must be respected. It is obvious that local contributing factors, such as significant refractive errors, should also receive proper attention. Prolonged cycloplegia and sedation seem to have small effect on the outcome of the disturbance.

A case is herewith presented which appears to satisfy the requirements essential for the diagnosis of hysterical convergence spasm. Observation during a period of one and one-half years has failed to cause alleviation of the condition in spite of attempted psychiatric therapy of "persuasion and countersuggestion."

REPORT OF A CASE

G. A., a 22 year old white woman, was admitted to the service of Dr. Francis Heed Adler at the Hospital of the University of Pennsylvania on Nov. 6, 1939 for the investigation of a disturbance of ocular motility of approximately ten months' duration. The patient's chief complaints were diplopia, vertigo and occasional occipital headache. The last-mentioned symptom was of long duration and had in fact been the basis for extensive study in the neurologic service of the hospital during May 1937. The result of this study, which included an encephalogram, was essentially negative. An ophthalmologic examination at this time disclosed myopia and depression of the peripheral fields of vision, but the eyes were considered to be without relation to the patient's symptoms. Headache continued without abatement during the two years which followed the patient's discharge from the hospital. During this period the patient was under constant supervision of an ophthalmologist in another city, who prescribed prismatic lenses for correction of a "muscle imbalance" and later conducted a three months' course of orthoptic training exercises for the same purpose. The patient volunteered the fact that she had experienced great difficulty at first in recognizing double images with one of the common types of orthoptic instruments.

Several months after the conclusion of this course of treatment the patient began to notice periods of diplopia associated with vertigo. These symptoms continued and increased in severity until her admission to the hospital in November 1939. During the same period headache became a much less noticeable symptom than it had been previously.

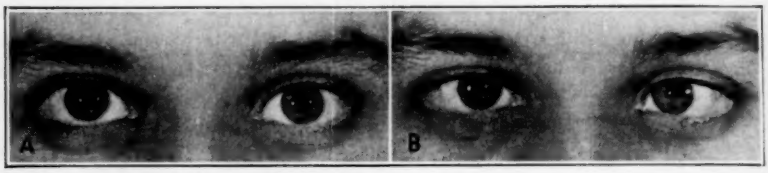
It has been stated that diplopia was the patient's principal difficulty at the time of admission to the hospital. This symptom was noted when she looked at any object for a short time at a near or distant point. The patient suggested that diplopia could be made to disappear when she ceased to fix upon an object.

Taking of the patient's medical history evoked the admission that she had been ill most of her life. She qualified this statement by explaining that she was subject to frequent minor ailments. No serious difficulties were encountered, however,

until she reached the age of 16, when, after several months of dysmenorrhea, a bilateral salpingo-oophorectomy was performed in another city for a condition diagnosed "cystic ovaries." Menses ceased, of course, after this procedure, but no severe menopausal symptoms developed. In 1939 the removal of an impacted wisdom tooth was accompanied by a period of lethargy which persisted for two weeks. During this period the patient experienced the sensation that her "jaws clamped shut." Her family physician informed her that she was on the verge of a nervous breakdown, but the event was evaded by complete rest in bed for a short period. No other significant points were uncovered in the medical history.

A social history indicated that the patient's childhood was normal. She graduated from high school with honors at the age of 16 and was thereafter employed as a department store pianist until illness forced her to resign. She denied sexual difficulties. She said that she had been disappointed when she first learned of her sterilization, but she later assumed the attitude that this fact did not contraindicate marriage. Her relationship with men was extremely limited, a fact which she claimed was due to discouragement on the part of her parents.

Her home life was unhappy, especially with regard to her relations with her mother. She expressed irritability toward her mother, and she also felt that her father showed favoritism toward her sister. She expressed some satisfaction in the fact that her father's attitude toward her improved when she became ill.



A, normal appearance of patient's eyes. *B*, patient's eyes during convergence spasm. Note the intense miosis.

No significant data were uncovered in the patient's family history.

At physical examination on admission the patient was intelligent and cooperative and showed an objective, unemotional interest in her illness. The significant points disclosed were atrophy of the breasts and absence of the pelvic adnexa.

The ophthalmologic examination revealed at once a confusing disorder of ocular motility. A transient convergent squint of variable angles was observed at frequent intervals (*B* in the accompanying illustration). It reached greatest magnitude when the patient was asked to fix on a near object but was also readily visible when she regarded a distant object. The act of convergence was accompanied by the complaints of diplopia and vertigo. Partial blepharospasm was apparent in one or both eyes and suggested the patient's attempt to suppress diplopia. When the patient was instructed to stare blankly into space the visual axes soon returned to their normal positions. Extreme miosis was invariably associated with the excess of convergence. A test of binocular ocular rotations at the near point suggested paresis of both external rectus muscles, but this impression was refuted by the presence of full monocular rotations.

Visual acuity without correction was 6/30 in the right eye and 3/60 in the left eye. In the right eye, with a correction of -0.75 D. sph. $\supset -0.37$ D. cyl., axis $30 \supset 1.5^{\Delta}$ base down, 6/6 vision was obtained. In the left eye, with a correction of -3.00 D. sph. $\supset -0.50$ D. cyl., axis 150, 6/9 vision was obtained. Studies of the muscle balance were unreliable owing to an extreme variability of the ocular

rotations, but right hyperphoria of 1 prism diopter was indicated on several occasions.

Studies of the visual field demonstrated a moderate depression of the peripheral portion (at 33 cm.), but the central portion at 1 meter disclosed no abnormality with a 2 mm. white test object. An ophthalmoscopic examination indicated moderate myopic changes in both fundi.

Retinoscopic examination without cycloplegia during a period of convergence excess uncovered between 8 and 10 D. of myopia, and lenses of these powers produced marked clarity of double images. With atropine cycloplegia the following retinoscopic result was obtained: right eye, —0.50 D. sph. ⊃ —0.25 D. cyl., axis 30; left eye, —2.00 D. sph. ⊃ —0.50 D. cyl., axis 15. It is certain that the disparity in the result of the two examinations was produced by excessive accommodation, which was possible before cycloplegia was obtained.

Laboratory studies gave essentially negative results except to disclose a mild degree of secondary anemia. The basal metabolic rate was —13 per cent.

A neurologic consultant (Dr. George D. Gammon) concluded an unproductive examination by suggesting the remote possibility of myasthenia gravis as the basis for the disturbance in ocular motility. This diagnosis was excluded with a therapeutic trial of prostigmine, which was given subcutaneously without effect.

A psychiatrist (Dr. Louis E. Twyeffort) was consulted after no organic basis for the patient's ocular difficulties could be discovered. The psychiatric examination disclosed considerable evidence pointing toward psychoneurotic factors in the patient's illness, but the specific connection between these factors and the ocular spasms could not be brought out. The following psychiatric impression was offered: "Spasm of ocular convergence in a young person showing a few specific neurotic trends (anxiety elements and hysterical elements)."

Treatment during the patient's hospitalization consisted of atropinization of both eyes and sedation with small doses of phenobarbital. Overcorrection of the patient's existing myopia was rectified by prescribing the correction obtained with atropine cycloplegia. The patient was discharged from the hospital November 17 to the care of her family physician, who was instructed to administer ovarian replacement therapy as well as small doses of thyroid substance to combat a slight hypothyroid state. The use of barbiturates also was suggested.

The patient has shown no remission in her illness. Convergence spasm can be readily elicited at the time of writing (June 1941), although the subjective aspect of the disturbance has diminished to the point of being a minor annoyance in the train of symptoms. The absence of organic abnormality of the eyes has been repeatedly stressed to the patient. Suggestions regarding change of environment and the development of new interests have met with the patient's refusal.

COMMENT

A case of hysterical convergence spasm is reported. The disease represents an excess of convergence, usually associated with a comparable excess of accommodation, which becomes pathologic because of its duration and severity in susceptible, psychoneurotic patients. Suggestion probably plays a prominent part in the causation of the disease, and it is in this connection that orthoptic training exercises might in some cases be incriminated. It may be supposed that this type of therapy presented a new outlet for a long-standing psychoneurosis in the patient whose case is reported.

PARALYSIS OF THE SUPERIOR RECTUS AND THE INFERIOR OBLIQUE MUSCLE OF THE SAME EYE

JAMES WATSON WHITE, M.D.
NEW YORK

Paralysis of both elevators of one eye, although one of the less common paralyses, is seen not infrequently and is generally if not always congenital. The paralysis of both muscles is more or less well defined; usually the inferior oblique is the more paretic of the two.

Such paralysis limits elevation throughout the whole upper field, in the temporal field owing to the underaction of the superior rectus muscle and in the nasal field owing to the underaction of the inferior oblique muscle.

There may be true ptosis or pseudoptosis accompanying the paralysis. The true ptosis is due to paralysis of the levator muscle. The pseudoptosis is brought about because the lid of the paretic eye follows the eye down much as both lids do normally when the eyes are fixating in the lower field. Either true or false ptosis may be exaggerated in order to prevent diplopia.

The exact cause is uncertain in most cases, but the history of difficult labor and especially of forceps injuries is too frequent to be disregarded.

One patient had a long flabby inferior oblique muscle lying loose, almost coiled on the floor of the orbit. In no patient on whom I have operated has either muscle been absent.

The secondary deviation, which can usually be demonstrated by the screen comitance test, would tend to disprove the theory of a complete lack of innervation or an agenesis of the centers in the third nerve nucleus.

The anomaly is seen in three different varieties: first, that in which binocular single vision is maintained, usually by a backward tilting of the head to get the image more in the field of the depressor muscle; second, that in which fixation is with the nonparetic eye when the paretic eye is in a position of hypotropia (it is in this type that the ptosis, either true or false, is the most marked); third, that in which fixation is with the paretic eye (here the sound eye has a marked secondary deviation,

Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

which makes the deformity much more disfiguring than that accompanying either of the other varieties).

In the first type the vision is usually equal and normal or made so by correction of an existing ametropia. To prevent diplopia the head is tilted backward. With the head held in the primary position diplopia may be readily charted. In pronounced paralysis the measurements cannot be accurately determined by cover test or by diplopia charts, since the eye cannot be elevated enough to make this possible. In fact, the results of the screen comitance test are most valuable in the appraisal of all three varieties. When the paralysis is less pronounced measurements may be made by means of the screen (cover) test or by mapping the diplopia.

In the second type vision in the paretic eye is below normal, often 20/200 or less. The paretic eye is in the position of hypotropia. The screen comitance test is most dependable.

In the third type the vision in the paretic eye is normal or made so by correction of an existing ametropia, while the vision in the nonparetic eye may be 20/200 or less.

To determine the ptosis in any type the palpebral fissure of each eye should be measured in millimeters while the fellow eye is covered.

Surgical intervention is indicated in all cases unless binocular fixation can be had without a definite head tilt and the deformity is not a cosmetic blemish.

The correction of any real ptosis should be postponed until the eyes have been brought to the same level. This is a point often overlooked, and its neglect is the reason for the unsatisfactory operative results from any type of operation for ptosis. One patient observed had had four unsuccessful operations for ptosis. The operations depending on the utilization of the superior rectus muscle should never be considered, owing to the weakness of this muscle.

When operating for type 1, one may resect the inferior oblique muscle at its origin or, better, tuck it near its insertion, according to the method I have described, following much the technic given by Wheeler [1] for tucking the superior oblique muscle. The approach is made below and to the outer side of the insertion of the external rectus muscle. The inferior oblique is brought up through the conjunctival incision and a tuck sutured with white silk. After the inferior oblique muscle is tucked, the superior rectus is shortened by an operation of the surgeon's choice.

The same procedure is followed for type 2, but there is little hope of producing binocular single vision and the operation is usually performed for cosmetic reasons only.

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1. Wheeler, J. M.: Advancement of the Superior Oblique and Inferior Oblique Ocular Muscles, Am. J. Ophth. **18**:1 (Jan.) 1935.

In type 3 the deformity is caused by the secondary deviation of both elevators of the nonparetic eye. A tenotomy or recession of the overacting superior rectus and the inferior oblique muscle gives a satisfactory cosmetic result. After the eyes are approximately level, any ptosis may be corrected as a final step.

When the paralysis is classified in this way and treated as outlined the results are most satisfactory.

ABSTRACT OF DISCUSSION

Dr. John B. Hitz, Milwaukee: I am greatly honored to have the opportunity to appear on this program in association with two such great leaders in American ophthalmology as Dr. White and Dr. Lancaster. Dr. White has presented his subject with his usual masterful simplicity.

Paralysis of both elevator muscles of an eye as a congenital phenomenon or one occurring early in life is apparently not particularly rare. I have observed 3 cases in a relatively small clinic within the past year.

Case 1.—The patient, A. M., was a girl aged 8 years. The onset had occurred two years (questionable) before. There was no history of injury at birth, and the family history disclosed nothing relevant. There was limitation of the movement of the right eye both up and out and up and in. Binocular vision was present in all fields except the right upper, in which the child fixed with the nonparetic eye. The vision was 20/20 in each eye. There was no ptosis, no head tilt and no manifest diplopia, but diplopia was easily elicited with red glass.

This illustrates type 1 in Dr. White's series.

At this point it might be well to mention that in my experience few patients with the type of congenital palsy under discussion show manifest diplopia. Such children seem to be able to suppress one image when the eyes move in the direction of the action of the weak muscle. However, diplopia can usually be elicited easily with the red glass.

Case 2.—J. P., a boy aged 5½ years, had the condition at birth. There was a history of a difficult labor; there was no family history of strabismus. There was definite palsy of the left superior rectus and the left inferior oblique muscle with associated pseudoptosis. The patient fixed entirely with the nonparetic eye. The vision was 20/20 in the right eye and 20/30 in the left. There was no head tilt or diplopia.

This case seems to illustrate type 2 in Dr. White's series.

Case 3.—The patient, F. M., was a girl aged 3 years. The family history was significant. The condition, present at birth, appeared to be definite bilateral paralysis of the elevator muscles with pronounced bilateral ptosis. In spite of the patient's having worn crutch glasses with reasonably good success for the past year, there was no demonstrable action of any of the four elevator muscles, although the lateral movements and the downward ones appeared adequate. The child's mother showed no ptosis, but in spite of having binocular vision in the primary position she was unable to move her eyes in any direction more than 5 degrees. Unfortunately, opportunity for further study of these cases has not yet presented itself.

In regard to measuring the deviation in such cases, I believe that the neutralization of movement in the six cardinal directions by the use of the cover test and prisms cannot be overemphasized. This applies to strabismus in general as well as to the cases of frank paralysis. Many times one will uncover a vertical deviation, in addition to the lateral, which may be on a paretic basis and may be responsible for the more obvious lateral deviation.

The study of binocularity of the vision would seem to be most important. Although the operative procedures selected may be the same, the approach to the problem is different, depending on whether one is attempting to reestablish binocular vision in the most usable directions of gaze and thus eliminate a head tilt or whether the correction is purely a question of appearance. If no binocularity is apparent and double images can be elicited, a check on the presence of anomalous retinal correspondence is indicated.

I should like to ask Dr. White whether any of his patients showed Bell's phenomena, which would indicate a supranuclear paralysis, and also what he thinks of Chavasse's theory that in many cases the condition is originally paralysis of the opposite trochlear nerve with development of relative comitance and so-called inhibitional palsy of the contralateral elevators.

DR. WALTER B. LANCASTER, Hanover, N. H.: I wish to call attention to diagnosis and treatment. The diagnosis can be facilitated a good deal by the red-green test (Lancaster, W. B.: ARCH. OPHTH. 22: 867 [Nov.] 1939), which makes it possible to examine in all the cardinal positions rapidly and accurately. For instance, if the elevators of one eye are both weak—even totally paralyzed—then with the red-green test, when the patient fixing with the paralyzed eye is told to fixate upward to right or to left, that eye cannot move up but the other eye greatly overshoots, and, conversely, if the nonparalyzed eye fixates, it follows the fixation light easily but the other eye, being paralyzed, lags behind, giving a simple, easily understood, positive diagnosis by direct reading of results, without complicated interpretation.

In the early stages of paralysis of one of the vertical muscles, there is a pronounced difference in the deviation whether the eye is in adduction or abduction, the vertical rectus muscles acting in abduction and both oblique muscles acting in adduction. However, it is also characteristic of paralysis that as time goes on deviations tend to become concomitant. This is obvious in the horizontal deviations. A paralysis of the abducens nerve of the left eye at first is apparent only when the patient looks to the left, but by and by there is a deviation all the way across, and this is nearly equal whether the patient is looking to the right or the left. In the case of the vertical muscles one gets a similar final effect of concomitance. Suppose one of these muscles, for example the right superior rectus, is paretic. At first the deviation will appear when the patient looks to the right and up, because that is the field of action of this muscle, but as time goes on there will be a deviation to both the right and the left, making it difficult to analyze the condition without a history of the deviation in the early stages. Fortunately there is a method which usually succeeds. That method is to judge the effect of tilting the head toward the shoulder. If there is any horizontal devia-

tion one must use the bite apparatus advocated by Bielschowsky (Lancaster, W. B.: ARCH. OPHTH. 22: 867 [Nov.] 1939) to do this, but if there is no horizontal deviation one can do it quickly with the red-green test. One finds, for instance, that if the right superior rectus muscle is paretic, if the head is tipped toward the right the vestibular apparatus makes the eye tilt toward the left, and this levocycloversion is done for the right eye by the superior rectus and the superior oblique muscle. If the superior rectus muscle is paretic, the superior oblique has to do the tilting alone, and the superior oblique not only does levocycloversion but does downward rotation so that the result is a downward vertical deviation increased by tipping the head toward the right shoulder. It would take too long to elaborate the technic fully.

A few words about the treatment. The same principle of eventual concomitance applies to operative treatment. If one tenotomizes the inferior rectus muscle of the right eye the main effect at first is when the eye is in abduction, but before long it will be found that the effect is distributed all the way across from adduction to abduction; so one can get a good effect by operating on only one of the vertical muscles. This is well shown in the average case of small hyperphoria, hyperphoria for example of 5 prism diopters. Even if the hyperphoria is caused originally by some muscular paresis, in the vast majority of cases it will be found to be about the same whether the patient is looking to the right or to the left, i. e. in either adduction or abduction.

DR. HERMANN M. BURIAN, Hanover, N. H.: Last week I examined a patient about whom I should like to have Dr. White's opinion as to whether or not I am dealing with a paralysis of both elevator muscles.

The patient is a 39 year old clerk in a machine shop whose family history contains nothing significant and who has never been seriously ill. He had worn glasses for twenty years, but a muscle disturbance had never been diagnosed.

Ever since he can remember he has had severe ocular fatigue, frontal headaches and photophobia on close work, but especially when watching moving objects. Frequently he sees double. The visual acuity is 20/15 in each eye with correction. The eyeballs show pathologic change.

The patient has full binocular vision and good fusional amplitudes, but as soon as one eye is covered even for a few seconds a vertical tropia and diplopia set in. In the primary position there is right hyperphoria of 13 to 15 arc degrees, about 30 prism diopters. In supraversion the right hyperphoria increases to 22 arc degrees; in looking down it decreases to 3 arc degrees. In looking to the right it is somewhat less than in the primary position. In looking to the left it is the same or slightly more than in the primary position, but the differences are not significant. In looking up and to the right there is 12 to 13 degrees of right hyperphoria; in looking up and to the left, 18 to 20 arc degrees of right hyperphoria.

This patient doubtless has a paralysis of the elevator muscles of the left eye. The question is whether both elevator muscles are primarily affected, or one of them. The fact that the right hyperphoria is very large both when the patient looks up and to the right and when he looks up and to the left may lead one to assume that both elevators are primarily affected, although the involvement of the superior rectus

muscle is undoubtedly predominant. Other facts, however, seem not to bear out this assumption.

In the head tilting test, when the patient's head is tilted to the left there is right hyperphoria of 15 arc degrees, indicating a weakness of the left superior rectus muscle. When the patient's head is tilted to the right, the right hyperphoria is reduced to 7 or 8 arc degrees, whereas if the inferior oblique muscle were paretic the right hyperphoria would be increased, not decreased. Also, in determining the position of the vertical meridian of the retina of the left eye, I found a disclination of 4 arc degrees, also indicating a paralysis of the left superior rectus muscle, not of the left inferior oblique.

I am inclined to draw the conclusion that this case is an instance of paralysis of the left superior rectus muscle which has tended to become concomitant, although there is no contracture of the antagonists.

Therapeutically, I propose a resection and advancement of the left superior rectus and a resection of the right inferior rectus muscle.

DR. JAMES W. WHITE, New York: The first discusser spoke of measuring in the six positions. With complete paralysis one cannot measure with the eyes in the up and to the left and in the up and to the right position because the eyes cannot move to these positions. The screen comitance is the only test one can depend on; so, as I brought out in my paper, diplopia tests, the Lancaster red-green test and all other tests are useless in cases of pronounced paralysis, because the eye cannot be elevated above the horizontal line much, if any.

A word in regard to the mistakes I have seen. So many operators use the superior rectus muscle to aid them in their correction of ptosis before they operate to bring the eye up. They use the superior rectus and attempt to correct the ptosis before correcting the difference in level. Any such operation hangs a big heavy lid on an already weak superior rectus muscle, and I have seen many patients, for example one who has been operated on four times and another operated on twice, in whom there was no improvement of the ptosis.

In regard to hyperphoria and hypertropia, the amount of vertical deviation does not make the distinction. I have seen a patient with hyperphoria of 30 degrees and another with hyperphoria of 20, while 1 or 2 degrees may constitute hypertropia.

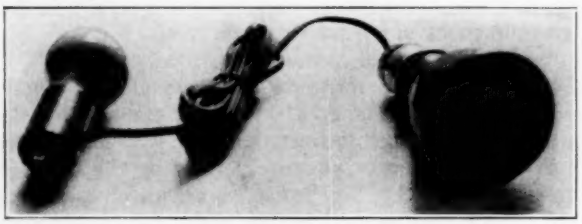
Clinical Notes

A SIMPLE INEXPENSIVE LAMP FOR FLUORESCENCE

BENJAMIN FRIEDMAN, M.D., NEW YORK

Interest in the phenomena of tissue fluorescence caused me to seek a fluorescent lamp which would eliminate some of the disadvantages present in the mercury vapor models. It was found that a small commercial unit built by the Stroblite Company, of New York, answered most of the requirements with the exception of adequate intensity. By increasing the energy output a highly satisfactory lamp has been obtained.

The source of radiation is a standard 2 watt argon glow lamp. This is enclosed in a small reflecting housing, with a heat-resisting purple filter. Eighty-eight per cent of the emergent rays possess a wavelength of 3,650 millimicrons. Only a small amount of visible light is emitted.



Small fluorescent lamp.

The resister in the base of the bulb was removed, and for it was substituted a 25 watt mazda blue bulb placed in series within the circuit; this had the effect of quadrupling the fluorescent power of the unit. The housing is about as large as a coffee cup, is easily handled, is light and may be brought right up to the eye. Since fluorescence follows a function of the square of the distance, the power of the lamp is strong in close proximity. The housing heats up slightly. The bulb operates on either direct or alternating current and is replaceable at a cost of 50 cents. It requires no heating-up period and is instantly ready for use. No transformer is needed. The whole outfit occupies little space in a handbag. The cost of materials and labor is about $10.

Examination of clinical subjects by means of the fluorescent lamp discloses some interesting findings. The small pinguecula fluoresces with a brilliant blue-white luster and if very small may be discovered by this means when natural observation fails to reveal it. The larger, fatty-looking pinguecula assumes a slightly yellowish glow, and this is intensified to a remarkable degree in the pinguecula of Gaucher's disease, which becomes irradiated with a beautiful chartreuse-colored luminescence.

The normal sclera fluoresces with a porcelain-like bluish glow, and, curiously, the luster is continuous even over the scleral dehiscenses seen in the "scleral plaques" described by Graves. In ordinary light the choroidal pigment in cases of such plaques is clearly seen through the gaps in the sclera, but when the lamp is employed the pigment is difficult to observe because of the fluorescence of unsuspected and otherwise invisible scleral remnants.

In the skin, areas affected by vitiligo, ringworm and flat verrucae glow with a bluish light. Scar tissue appears dark purple.

If fluorescein is given by mouth the sclera takes on a golden glow. In areas of episcleritis the glow is accentuated, but in areas of subconjunctival hemorrhage in which no circulation is present the golden glow is not discernible, nor is it noted when there are subcutaneous extravasations of blood. The same glow was evident around the borders of an induration of the arm which followed an injection of staphylococcus toxoid; the fluorescein appeared not to have been delivered to the central area because of circulatory stagnation.

The scalp and the lids become suffused with a similar golden color, and this is more marked in eczema of the lids.

I have found that fluorescein is transmitted to the secretions of the lid in cases of vernal catarrh. I have been unable to recover the dye in the secretions of purulent conjunctivitis.

The apparatus was constructed for me by Mr. Myron Drachman, M.E., of 69 Tieman Place, New York.

PREPARATION OF SULFATHIAZOLE OR SULFANILAMIDE OINTMENT

N. C. Elvin, M.D., Brooklyn

Before sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) or sulfanilamide is added to an ointment base, the powder should be sifted and a paste made with an equal amount of boiling water.

BASE 1

To 4 parts of sodium alginate add 75 parts of boiling water; emulsify and strain, and then stir until cool. Add 16 parts of anhydrous wool fat, 78 parts of white petrolatum and 1 part of sodium chloride dissolved in 4 parts of water.

BASE 2

Sodium lauryl sulfate	½ part
Cetyl alcohol	8 parts
Theobroma oil U. S. P.	6 parts
White petrolatum	20 parts
Water	65 parts

Use a water bath to melt the first four ingredients and then add water, stirring constantly.

BASE 3

Liquid petrolatum	35 parts
Spermaceti	13 parts
Glycostearin	10 parts
Water	38 parts

Heat the first three items to 140 F. Add them to the water at the same temperature, stirring constantly.

Base 1 is not irritating and is best for ophthalmic use, although the others may be used.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

EYESIGHT IN INDUSTRY

LEO L. MAYER, M.D.
LOS ANGELES

PRIME IMPORTANCE OF EYESIGHT IN INDUSTRY

Industrial efficiency depends on good vision. The employer who is concerned with the welfare and health of his employees reaps a tangible reward in work well done. The employee, likewise, gains for himself a knowledge of his capacity and proper care of his disabilities. The correction of defective vision, the maintenance of lighting conditions appropriate to the work performed and the protection of the eyes in hazardous occupations, all these are necessarily of concern to industrial managements.

The purpose of this article is to acquaint those persons who are interested with the many phases of vision and the factors concerning the eye of the employee from the standpoint of the eye physician and surgeon, the ophthalmologist. So far as I have been able to discover, no comprehensive and thorough contribution of this nature has ever been written. It is, however, true that a survey of the available literature reveals many short or incomplete articles on various phases of the eye in industry. Many of these have been consulted in the preparation of this monograph, and proper credit and reference will be given for those used.

BACKGROUND FOR EXAMINATIONS OF THE EYES

Statistics are at hand to give some idea of the prevalence of impaired eyesight in large classes of presumably healthy persons, many of whom are entirely unaware of having defective vision. In modern times, especially in the larger communities, the school child has a perfunctory test of vision, and in many cases proper care is supplied. However, it is characteristic of the human animal that when known defects cause no discomfort in the eyes they may be forgotten or dismissed. Certainly it is true the young adult looking for his first position is usually unconcerned about his eyes, which are not incapacitating him.

Examination of the three million men drafted for service in the last World War showed that about 3 per cent had poor vision.[1] Curiously

1. Love, A. G., and Davenport, C. B.: Defects Found in Drafted Men, United States War Department, 1920, p. 40.

enough, the highest incidence of defective vision occurred among men from large cities.

The Metropolitan Life Insurance Company [2] has given details of numerous examinations of the eyes in industry, and I quote verbatim:

> Matthew Luckiesh, Director of Lighting, Research Laboratories, General Electric Company,[3] has prepared an interesting table, based on a study of nearly a million subjects, which shows the increase in the number of visual defects with age and the comparative ratio of these defects in school children, college students and industrial workers.
>
> An eyesight survey among industrial workers, taken from the records of 40 companies by the Eyesight Conservation Council,[4] revealed an average of 44.3 per cent with defective vision. The range extended from 10.6 per cent of workers in telephone companies where the average age of the personnel was young, and where those with defective sight were presumably largely excluded through the strict physical examination on entrance, to 79.1 per cent in the men's clothing industry.
>
> A more recent survey of the eyesight of adults, however, is found in the analysis of over 100,000 examination records of insured males during the past eight years.[5] The corrected and uncorrected visual defects (eyesight less than normal in either eye according to Snellen or Jaeger tests) were analyzed by ages and by occupational groups. Defective vision was found in from 21.0 per cent of agricultural workers at ages 20-24 to 78.2 per cent at ages 55 and over. For business and professional men, defects were present in from 36.4 per cent at ages 20-24 to 83.4 per cent at ages 55 and over. For workers in skilled trades, defects were present in 29.0 per cent at ages 20-24 to 77.6 per cent at ages 55 and over.
>
> There was evidence, therefore, that professional and business men have the highest incidence of defects in the younger age groups, that skilled industrial workers form the intermediate group, and that the lowest percentage of defective eyesight is found in agricultural workers. At the older age groups, above 50 (the age of physiological change), the incidence of defects in the four groups becomes more uniform while at the same time it is consistently higher. These figures, however, are based only upon the percentage of defects found, and do not take into account the severity of the defects. It is probable that the sedentary life of the office worker with its consequent lowered muscle tone results in a greater number of deviations from so-called normal sight due to small errors of refraction than is found in out-of-door workers.
>
> It is also notable that a consistently higher percentage of skilled workers, in whom accurate eyesight is presumably valuable to themselves and to their employers, allowed defects to go uncorrected than did any of the other groups.
>
> In an analysis of approximately 5,000 applicants for employment, whose average age was 21 years, covering an experience of years of compulsory eye examina-

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2. Functions of an Industrial Eye Clinic, Industrial Health Series, no. 4, New York, Metropolitan Life Insurance Company, 1931.

3. Luckiesh, M., and Moss, F. K.: The New Science of Seeing, Tr. Illum. Engin. Soc. **25**:15, 1930.

4. Eyesight Conservation Survey, Bulletin 7, New York, Eyesight Conservation Council of America, 1925, p. 82.

5. Sydenstricker, E., and Britten, R. H.: Physical Impairments and Occupational Class, Pub. Health Rep. **45**:1927, 1930.

tions at the Eastman Kodak Company, it was found that about 13 per cent needed glasses and 40 per cent of those wearing glasses needed to be refitted. In a group of older employees, 71.3 per cent were found to have defective vision.[6]

It is the chief purpose of this booklet to indicate the benefits resulting from correcting defective eyesight and to suggest methods of supervising the visual condition of the workers through industrial plant clinics.

Rainey [7] found in the examination of 15,000 employees 2,100, or 14 per cent, who had vision of less than 100 per cent in one or in both eyes. Thacker [8] in an examination of students at the University of Illinois found that 34.3 per cent had defective vision. Shaffer,[9] of the Bethlehem Steel Company, reported that 46 per cent of all rejections were because of defective vision. Schereschewsky [10] found that 75 per cent of garment workers had some defect of vision. From these scattered reports it is readily understood just why industries must take cognizance of the working ability of the eyes of their employees.

LABORATORY CONTRIBUTIONS

ILLUMINATION

In addition to the actual practical examinations of the eyes of employees in industry, much work of a scientific nature has been accomplished to supply basic fundamentals. A great portion of this work has been evolved and cited by Luckiesh, director of lighting research at the General Electric Company. Luckiesh and his workers are most naturally interested primarily in lighting but nevertheless have contributed to the questions of fatigue, rate of production, conservation and measurements. In the preface to the book by Luckiesh and Moss [11] the opening paragraph is worthy of reproduction:

> Seeing is more than visual function. It is an activity of the human being. As such it is subtly, intimately and almost universally woven into the complexity of civilization. It is not only an important part of the foundation of modern life, but it extends prominently throughout this structure and ramifies into much of the embellishment of living. It is a vast panorama including external physical factors, phenomena of the visual sense, psychophysiological effects, and human limitations, abilities and achievements. The science of seeing encompasses controllable aids and hindrances to seeing, internal penalties and rewards to the

6. Findings After Seven Years' Experience of Compulsory Examination of the Eyes of Employees, abstracted, Am. J. Pub. Health **21**:297, 1931.

7. Rainey, C. W.: A Visual-Acuity Survey: Report of Seven Hundred and Twenty-One Cases, Am. J. Ophth. **20**:930, 1937.

8. Thacker, E. A.: A Study of Ocular Defects Among University Students, Am. J. Ophth. **22**:1003, 1939.

9. Shaffer, cited by Davidson.[75]

10. Schereschewsky, cited by Hardy.[20]

11. Luckiesh, M., and Moss, F. K.: The Science of Seeing, New York, D. Van Nostrand Company, Inc., 1937.

human seeing-machine, characteristics and requirements of performance, and eventual efficiency, comfort, welfare and experience through the activity of seeing. It includes various sciences or aspects of organized knowledge as well as meagerly explored realms. Its boundaries in the external physical world are obvious but they also extend unobviously and deeply into the complexity of the human being.

In chart 1 are shown some of the major variables which influence visibility as depicted by Luckiesh and Moss. The great influence of the variation of illumination is shown by these authors in chart 2. The United States Public Health Service has been interested in the subject of illumination and its effect on postoffice employees. An increase in efficiency of 4.4 per cent with increased illumination has been reported.[12] It was also found that "there was a definite improvement in visual 'acuity' after the subject had worked under high illumination for a sufficient length of time, and a corresponding decrease after working under low illumination."[13] The effect on the working eye of variations in the intensity of illumination has been the subject of much experimental work by Ferree and Rand. As early as 1920[14] they stated: "It is fortunate too that the study of the effect of variations of intensity of light afforded an especial convenient, feasible and suggestive starting point for the testing of other functions of importance to the working eye." Later these authors[15] stressed the effects of variations in individuals, the group needs, the effect of glare, the placement of light, the placement according to individual needs and the types of lighting. Principles of good working conditions for the eyes were stated.[16] Eyestrain was defined as follows: "This striving to clear up its vision by ineffectual maladjustments is the cause of what is commonly called eyestrain, and an important cause of ocular discomfort." It was said:

A complete program for light prescribing should have the following features: Tests should be made of the subject's (a) preferred intensity of light, (b) his range of toleration for intensity for comfortable use of his eyes for the work he

12. Studies in Illumination: I. The Hygienic Conditions of Illumination in Certain Post Offices, Especially Relating to Visual Defects and Efficiency, Public Health Bulletin 140, United States Treasury Department, Public Health Service, 1924.

13. Studies in Illumination: II. Relationship of Illumination to Ocular Efficiency and Ocular Fatigue Among Letter Separators in the Chicago Post Office, Public Health Bulletin 181, United States Treasury Department, Public Health Service, 1929.

14. Ferree, C. E., and Rand, G.: The Effect of Variations in Intensity of Illumination on Functions of Importance to the Working Eye, Tr. Illum. Engin. Soc. **15**:769, 1920.

15. Ferree, C. E., and Rand, G.: Better Lighting for Workers, Personnel J. **15**:207, 1936.

16. Ferree, C. E., and Rand, G.: Intensity of Light in Relation to the Near-Point and the Apparent Range of Accommodation, Am. J. Ophth. **18**:307, 1935.

is most accustomed to do and for different types of work, (c) his susceptibility to glare and (d) his need for color correction.

It has been well known for many years that changes in the eye occur from birth to old age, especially in the lens and in the ability to accommodate. Ability to accommodate begins to wane at about the age of 40. The part illumination plays in loss of accommodation has been investigated by Ferree, Rand and Lewis.[17] They concluded that certain increases in illumination are necessary as the person grows older, that workers should be divided into groups with respect to age whenever

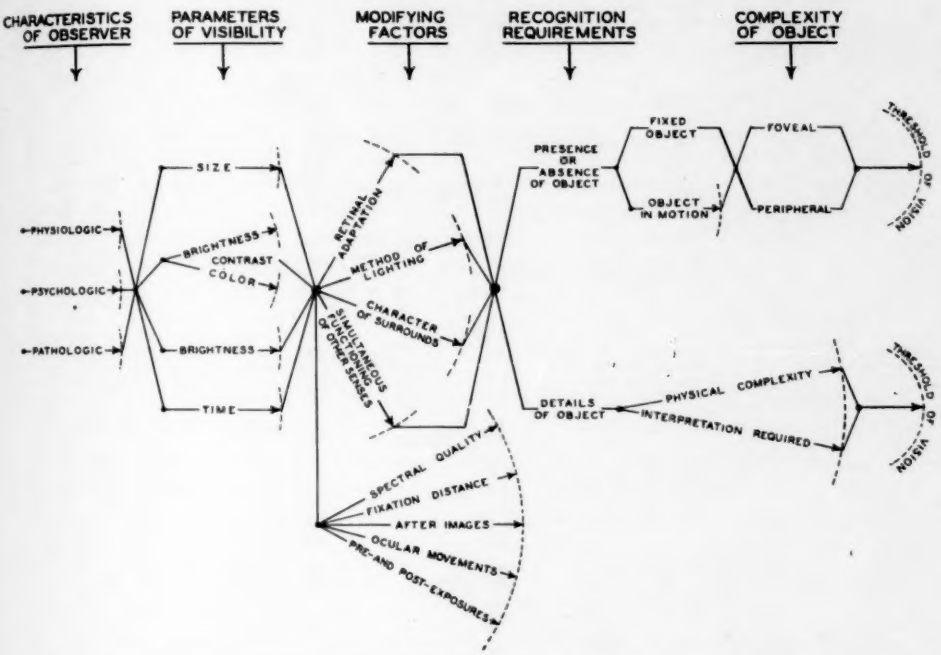

Chart 1.—The major variables which influence visibility. The human seeing Machine, located at the left, encompasses various human factors discussed in the text. (From Luckiesh and Moss.[11])

possible and that routine examinations of the eyes from a medical standpoint are necessary. Dr. Walter B. Lancaster, of Boston, is an ophthalmologist who for many years has been interested in lighting standards. In his report of the American Committee on Optics and Visual Physiology[18] many pertinent recommendations were made. It was found: "(1) That different individuals differ widely in what they

17. Ferree, C. E.; Rand, G., and Lewis, E. F.: Age as an Important Factor in the Amount of Light Needed by the Eye, Arch. Ophth. **13**:212 (Feb.) 1935.

18. Lancaster, W. B.: Lighting Standards, Am. J. Ophth. **20**:1221, 1937.

deem satisfactory lighting under various conditions. (2) That satisfactory lighting depends on other factors besides merely the brightness of the light falling on the work." The standards recommended for various occupations and locations were as follows: reading, 10 to 20 foot candles; sewing, 10 to 200 foot candles, depending on the color, contrast and fineness of the work, etc.; draughting, 20 to 50 foot candles;

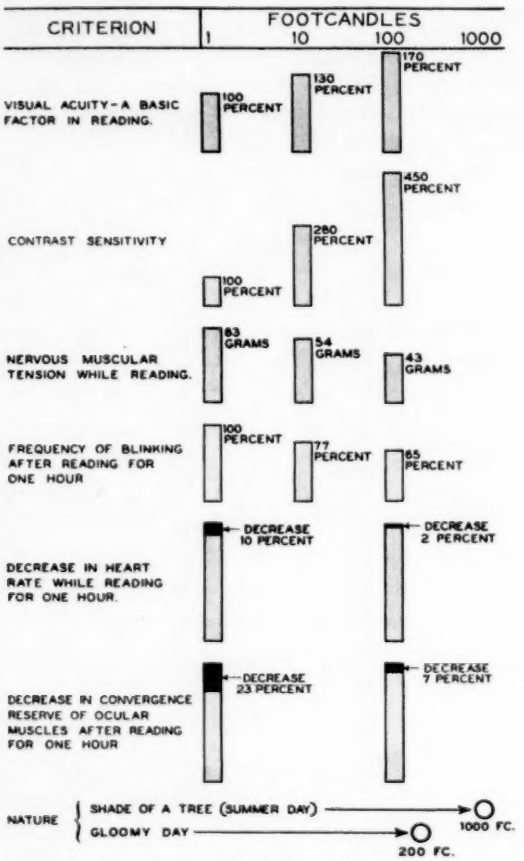

Chart. 2.—A summary of the results of extensive researches which revealed the influence of illumination on important aspects of visual acuity and on even more important effects of seeing. Researches dealing with these and other effects are revolutionizing the viewpoint from that of barely seeing to that of easy seeing. (From Luckiesh and Moss.[11])

auditoriums, 5 to 10 foot candles; locker rooms and toilets, 5 to 10 foot candles; stairs and corridors, 5 to 10 foot candles; ceilings, white or almost white, coefficient of reflection 75 per cent; upper part of walls, not shiny, coefficient 60 per cent; lower part of walls, neutral, coefficient 40 to 50 per cent; brightness of luminaires, not over 2 foot candles per

square inch. Later Lancaster [19] gave the following summary at a meeting of the Illuminating Engineering Society:

Comfort is subjective and cannot be measured objectively. It is negative rather than positive depending upon the absence of things that are irksome, painful. It depends very largely on habit and even fashion. Time is important since what is at first comfortable, may, if subjected to the ordeal of time, prove very uncomfortable.

Experience shows that what is conducive to efficiency, healthfulness and esthetic satisfaction will prove in the long run comfortable, when the inertia of habit and prejudice has been overcome.

The level of illumination most conducive to comfort can not be stated in definite figures of universal application because it depends on the eye (eyes with defects need more light), and on the task (more difficult and exacting tasks need more light).

Comfort is more likely to suffer today from poor distribution of light than from improper level of illumination. For comfort, light must be diffused. Individuals vary. Those with strong, healthy eyes, not overworked, are satisfied with any old light. For sensitive tests, sensitive eyes are needed. This is very important since many people can work with inadequate lighting without eyestrain, or even discomfort, but those with vulnerable eyes may suffer seriously. To attempt to set a definite standard in foot-candles is therefore to attempt the impossible. The illumination must be adapted to the task and to the peculiarities of those who are to perform it. The competent engineer will realize this and will make it clear to his clients.

L. H. Hardy, of New York,[20] summarized the following points in regard to illumination:

1. Defective illumination is a common and expensive cause of defective eyesight and accidents.

2. The major lighting defects may easily be recognized and in most cases eradicated.

3. The eradication of defective illumination is usually not only practically possible but economically profitable.

4. The best available statistics indicate that about 40 per cent of our industrial workers have defective vision due to ocular defects.

5. This number is probably being increased by unhygienic lighting conditions; and poor illumination augments the ocular deficiencies already present.

VISUAL ACUITY

Standard tests for visual acuity under proper illumination are well known. Certain laboratory and psychologic tests are of interest. Lythgoe [21] examined untrained subjects as to the certainty with which they

19. Lancaster, W. B.: Illumination Levels and Eye Comfort Conditions, Tr. Illum. Engin. Soc. **33**:964, 1938.

20. Hardy, L. H.: Illumination and Eyesight in Industry, Sight-Saving Rev. **11**:104, 1932.

21. Lythgoe, R. J.: The Measurement of Visual Acuity, Medical Research Council, Special Report Series, no. 173, London, His Majesty's Stationery Office, 1932.

saw an object of near threshold visibility. Each was asked to record when he was absolutely sure of seeing an object and when he was almost sure. For the former there were errors in 30 per cent of the cases; for the latter the error was 40 per cent.

If an object subtends a visual angle of 1 minute of the arc of a circle it is said to be visible to the eye. In other words, the object on the retina occupies a space in the neighborhood of 0.004 mm. Various investigators have made the determinations shown in the accompanying table, given by Adler.[22]

Thus it is readily realized that different persons vary in their acuity of vision.

Several so-called visibility meters have been produced for laboratory experiments. The Bennett-Casella [23] instrument alters the contrast of the object and its background. The Luckiesh-Moss type [11] uses a graduated wedge, and various tasks have been classified as to degree of ease of accomplishment according to this meter.

Resolving Power of the Eye

Author	Value in Microns at Retina	Visual Angle in Seconds
Lister	4.6	64
Hirschmann	3.6	50
Bergmann	3.8	52
Helmholtz	4.6	64
Uthoff	4.0	56
Cobb	4.6	64

The Section on Ophthalmology of the American Medical Association [24] approved the testing of visual efficiency according to the minute visual angle of the object.

That certain persons may actually increase the visual acuity of one or of both eyes has been demonstrated innumerable times by practicing ophthalmologists who have had occasion to give orthoptic treatments to cross-eyed children. Also, reading ability may be enhanced by practice, as has recently been shown.[25]

GLARE

Glare may be defined as a particular light source or reflection of a light source which because of its contrast and outstanding brilliancy over

22. Adler, F. H.: Clinical Physiology of the Eye, New York, The Macmillan Company, 1933, p. 128.

23. Bennett, M. G.: A Visibility Meter, J. Scient. Instruments **8**:122, 1931.

24. Report of Committee on Compensation for Eye Injuries: Appraisal of Loss of Visual Efficiency; Standard Method Approved by House of Delegates of the American Medical Association, Atlantic City, N. J., May 26, 1925, Tr. Sect. Ophth., A. M. A., 1925, p. 368; J. A. M. A. **85**:113 (July 11) 1925.

25. Vernon, M. D.: The Experimental Study of Reading, London, Cambridge University Press, 1931.

a background causes discomfort to the eyes. Needless to say, persons vary in their sensitivity to glare. Ferree and Rand [16] found the upper limits of light intensity for comfortable reading (expressed in foot candles) for 550 normal persons ranging in age from 10 to 77 years to be as follows: less than 5, 1 per cent of the subjects; 5 to 10, 11.3 per cent; 10 to 15, 26.5 per cent; 15 to 20, 20.8 per cent; 20 to 30, 17.7 per cent; 30 to 40, 8 per cent, and more than 40, 14 per cent.

Well known examples of glare are the reflection of the sun on snow, on a body of water and on a concrete road and the reflection of an unshaded light source or bright portion of a lighting fixture on glossy paper, paint and wood. Polished surfaces, such as metal automobile headlights at night, may cause glare. Since various criteria have been used to appraise the effects of glare, much in the investigative field may be reported from the literature. Cobb and Moss [26] noted the dire effects on visibility caused by glare. Holladay,[27] in testing visual efficiency with and without glare, demonstrated the marked reduction when glare is present. The discomfort and the increase in muscular tension were readily demonstrated by Luckiesh and Moss.[28] That both psychologic and physiologic factors need important consideration has been shown by the conclusions of Millar and Gray,[29] who expressed the opinion that glare affects comfort as much as if not more than visual efficiency does. A test for glare demonstrated by Lancaster [18] has simplicity and effectiveness. It consists in holding a pencil parallel to a sheet of paper and about 3 inches (about 7 cm.) from it. The paper is held so that the light falls perpendicularly on it. If the light is diffuse the shadow is blurred. If the shadow is fairly sharp and clearcut the light is not diffuse but is concentrated and not agreeable for reading.

The effect on the retina, with production of lasting after-images, caused by glare in reducing central visual acuity is a phenomenon known to every one. An outstanding piece of practical testing in regard to this problem is that of Spaeth.[30] The request came from the National Brotherhood of Railway Firemen and Enginemen. Firemen, whose duty it was to call track signals, claimed that it was impossible for them to

26. Cobb, P. W., and Moss, F. K.: The Four Variables of the Visual Threshold, J. Franklin Inst. **205**:831, 1928.

27. Holladay, L. L.: The Fundamentals of Glare and Visibility, J. Optic. Soc. America **12**:271, 1926.

28. Luckiesh, M., and Moss, F. K.: Muscular Tension Resulting from Glare, J. Gen. Psychol. **8**:455, 1933.

29. Millar, P. S., and Gray, S. McK.: Glare: Its Manifestations and the Status of Knowledge Thereof, in Proceedings of the International Commission on Illumination, 1928, p. 239.

30. Spaeth, E. B.: Light Adaptation at the Macula: Example of Its Industrial Importance, Arch. Ophth. **18**:248 (Aug.) 1937.

see the signals and call them properly after gazing at the intense illumination of the fire box for any length of time. It was found that they had to use perimacular, or indirect, vision to see signals because of the after-images produced at the macula after viewing of the fire box.

In addition glare causes increased activity of the pupil and iris muscles in shutting out an unnecessary light source. Even the subject's attempt to close the lids makes for excessive muscular action, with resulting discomfort and fatigue. The introduction of colored lights[31] does little to solve the problem of glare. Albers and Sheard[32] said:

> Three classifications of glare are commonly made: (1) veiling glare, the result of light uniformly superimposed on the retinal image which reduces contrast and, therefore, visibility; (2) dazzling glare, caused by adventitious light scattered in the ocular media so as to form part of the retinal image; and (3) blinding or scotomatic glare, which is produced by light of sufficient intensity to reduce the sensitivity of the retina.

In an investigation of 144 persons who had no complaint of being sensitive to light, these authors, using a unique glarometric method, found that the percentage having sensitivity for the right eye was larger than that having sensitivity for the left eye or for the two eyes together. Tinted glasses did not alter the relative values of the glare-out illumination. In a later study the same authors,[33] in investigating the tolerance of light in a group of patients with exophthalmic goiter, such patients being known clinically to be very sensitive to glare, found that they were 50 per cent more intolerant than the average normal person and also that after removal of the thyroid gland they approached the average normal person in sensitivity.

FATIGUE

Physical fatigue as a generalized term is difficult to define because of the innumerable factors concerned. However, one must not lose track of the fact that the eye, a single unit of the entire bodily makeup, is influenced by bodily fatigue and reciprocally has its influence on general bodily fatigue. Jackson,[34] who by reason of some sixty years of clinical service would seem most qualified to judge, expressed the belief that the most constant and general symptoms of visual fatigue are sensations of dryness, roughness, burning and smarting and a feeling as of a foreign body in the eye.

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31. Luckiesh, M.; Holladay, L. L., and Taylor, A. H.: Relative Glare in Moderately Colored Lights, J. Optic. Soc. America **11**:311, 1925.

32. Albers, E. C., and Sheard, C.: The Tolerance of Light in Nonphotophobic Individuals, Am. J. Ophth. **19**:407, 1936.

33. Albers, E. C., and Sheard, C.: The Tolerance of Light in Exophthalmic Goitre, Am. J. Ophth. **19**:460, 1936.

34. Jackson, E.: Visual Fatigue, Am. J. Ophth. **4**:119, 1921.

In a publication of the National Safety Council [35] it was said:

> Despite good illumination systems, eye fatigue occurs. There are instances where vigorous workers between 45 and 50 years old, who were apparently tired out at quitting time daily and whose earnings fell off without apparent reason (in some cases as much as 20 per cent) later exceeded their best record of production after being properly fitted with glasses.

Frank B. Gilbreth,[36] after many years of intensive study of this subject, estimated that the loss to American industry in production alone resulting from the fatigue of workers is more than 20 cents per day per worker, or more than $2,000,000,000 per year. This is at least four times the fire loss of the United States, and, like the fire loss, it occurs year after year. No one will deny that poor vision—whether due to insufficient light or to uncorrected ocular defects—is one of the principal factors in causing fatigue not only of the eye but of the entire body.

Lowered production is the most easily recognized result of fatigue. Another result is slowness to respond to stimulation. A workman who is fatigued does not see, does not hear, does not understand and does not act with his accustomed speed. For example, he may be working at a punch press and actually see the plunger descending on his fingers, yet slowness of reaction or of comprehension due to tired nerves will result in his failure to remove his hand in time to avoid losing several fingers. W. Murray,[37] engineering inspector of factories, London, England, made the following statement:

> Where work of a very fine nature is executed, it is not always possible to overcome the difficulty of seeing the work by illumination alone. If one attempts to see the fine details of the threads in woven silk, or artificial silk, or the fine wires used in wireless components, or even in burling and mending, it will be found that the object has to be held quite near to the eyes—say, some 6 to 9 inches—and many workers are now being provided with special magnifying spectacles. This problem was the subject of a special investigation by Mr. H. C. Weston,[38] of the Industrial Fatigue Research Board (now the Industrial Health Board) and is very ably explained in Report No. 49 on "The Relief of the Eye Strain among Persons Performing Very Fine Work," published by the Stationery Office. The principle employed is, in a measure, the use of magnifying lenses, and when these are properly and correctly fitted to suit the individual worker's

35. Reducing Fatigue, Practical Method for Safe Practices, Pamphlet 50; cited by Carris,[83] National Safety Council.

36. Gilbreth, F. B., cited by Carris.[83]

37. Murray, E. W.: Factory Lighting and Accident Prevention, Publication 241, National Society for the Prevention of Blindness, Inc., 1937.

38. Weston, H. C.: The Relief of the Eye Strain Among Persons Performing Very Fine Work, Medical Research Council, Industrial Fatigue Research Board, Report no. 49, London, His Majesty's Stationery Office, 1927.

normal vision, they afford a marked help to the operatives in reducing the fatigue of the eye caused by the angle of convergence and accommodation.[39]

Berens [40] said:

> Unsteady, variable and flickering illumination, forcing the eye to readjust itself constantly under the varying conditions of seeing, may also cause eye fatigue. Shadows caused by clouds and smoke may cause annoying variations in light. Flickering which results from a varying current is extremely tiring. Moreover, when the eye has been accustomed to a high degree of illumination during the day and natural light fails, making artificial light necessary, a higher level of illumination is usually required than at night under artificial lighting alone.

Luckiesh and Moss [41] stated the belief that the size of the pupil is indicative of the degree of ocular fatigue. They were able to demonstrate that the pupil is larger at the end of the day and also that the size increases as the week progresses and diminishes over the week-end. Tefft and Stark [42] demonstrated that the speed of accommodation is lowered by age, heterophoria, astigmatism, ametropia, low visual acuity and other visual anomalies and that fatigue thus ensues. Schubova [43] found that ocular fatigue induced by prolonged close work increases the time required to focus the eyes for clear vision. Tinker [44] has shown that visual fatigue (of ability to sustain clear seeing) increases when less than 3 foot candles of well diffused light is used for reading. There was no variation in fatigue with from 3 to 53 foot candles. He [45] also said:

> Visual fatigue and lessened efficiency are produced by brightness contrast within that portion of the visual field where critical vision is required and also within the immediate surroundings. When the eyes must shift back and forth from bright to dark areas or when there is a sharp division between dark and bright portions of the working area, the eyes must constantly re-adapt to the different degrees of brightness. Eyestrain soon results.

The eyelid reflex, i. e. blinking, has been used by numerous authorities as an indication of visual fatigue. Ponder and Kennedy [46] said that the

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39. Weston, H. C., and Adams, S.: The Effect of Eyestrain on the Output of Linkers in the Hosiery Industry, Medical Research Council, Industrial Fatigue Research Board, Report no. 40, London, His Majesty's Stationery Office, 1927.

40. Berens, C.: Eyes in Industry, Hygeia **16**:125, 1938.

41. Luckiesh, M., and Moss, F. K.: Size of Pupil as a Possible Index of Ocular Fatigue, Am. J. Ophth. **16**:393, 1933.

42. Tefft, L. E., and Stark, E. K.: Speed of Accommodation as a Practicable Test for Fliers, Am. J. Ophth. **5**:339, 1922.

43. Schubova, T. B.: The Effect of Ocular Fatigue on Sensitiveness to Differentiation, Am. J. Ophth. **17**:178, 1934.

44. Tinker, M. A.: Illumination Standards for Effective and Comfortable Vision, J. Consult. Psychol. **3**:11, 1939.

45. Tinker, M. A.: Facts Concerning Hygienic Illumination Intensities, School & Soc. **47**:120, 1938.

46. Ponder, E., and Kennedy, W. P.: On the Act of Blinking, Quart. J. Exper. Physiol. **18**:89, 1927-1928.

rate of blinking is closely related to the mental tension of the subject. Litinskiy [47] studied school children while they were reading and noted a decided increase in the rate of winking as fatigue ensued. Luckiesh and Moss,[11] using the technic described by Peterson and Allison,[48] investigated blinking under the following experimental conditions: (1) during the first and last five minutes, respectively, of an hour of continuous reading; (2) during the reading of types of different sizes; (3) during reading with and without a glare source within the visual field: (4) during the performance of a visual task requiring rapid and alternate fixation of two different test objects, and (5) during reading while eyeglasses of *improper* prescription were worn. They concluded that the rate of blinking is increased without exception when the specific visual task is made more difficult or more prolonged. Other phases of ocular fatigue will be discussed in relation to the extraocular muscles.

EYE MUSCLES

The muscles which concern the eye and the function of seeing may be divided into three groups: (1) the facial muscles and those of the lids, (2) the extraocular muscles which turn the eyeball and (3) the muscles controlling the pupil and the accommodation of the lens. In the first group are those muscles which react like the entire musculature of the body, and hence a recapitulation of the laboratory work on them would be too enormous to consider here. Suffice it is to say that in general muscular disease the ability to close and open the lids is readily found to be affected. Likewise, in paralysis of the facial nerve involving the orbicularis muscle frank evidence of loss of ability to transmit impulse is noted by electrical and other tests. In addition, the fact should not be lost sight of that this muscular function plays a role in the protection of the eyeball and its tissues. The so-called corneal reflex, together with the visual perception of a foreign substance approaching the eye, takes into account the integrity of the sensitivity of the cornea, the visual acuity and the reaction of the protecting orbicularis muscles.

The second group, the extraocular muscles, have to do with turning the eyeball in various directions so that binocular fixation of an object is readily and easily accomplished. Laboratory methods of studying the efficiency and fatigability of these muscles have been in use for many years. Most of the investigative work has been directed to the study of convergence, as this act is of most interest and is necessary for binocular single vision for all close application of the eyes. In 1893

47. Litinskiy, G. A.: Recording of Winking as a Method of Study of Ocular Fatigue in Children Resulting from Reading, Sovet. vestnik oftal. **4**:275, 1934.

48. Peterson, J., and Allison, L. W.: Controls of the Eye-Wink Mechanism, J. Exper. Psychol. **14**:144, 1931.

Sherrington [49] showed that reciprocal innervation (which makes possible active contraction of one muscle with diminution of the activity of its antagonists) characterizes the extraocular muscles. The extreme complexity of even a straight lateral movement has been well defined by Duane.[50] Duke-Elder [51] expressed the belief that "any evidence of fatigue in vision is due to a functional failure of the ciliary muscle, a failure in the coordination of the extraocular muscles, or in the higher processes of attention and interest." In 1912 Howe [52] devised an instrument called an ergograph which by means of prism additions was able to measure the fatigue of an extraocular muscle. Also, it could measure the act of convergence of the eye in close work. Berens and his co-workers [53] continued Howe's work and also studied the fatigue of accommodation.

The tremendous impetus given to the science of orthoptics of recent years and the management of crossed eyes have greatly stimulated research into the extraocular muscle function. In addition, it is necessary to know that fusion and depth perception are closely linked to the question of binocular fixation and the ability to view an object singly with the two eyes. Fusion and stereopsis vary with the individual, and fatigue of these functions is greatly influenced by general bodily health and by the type of work done.

Luckiesh and Moss,[54] while primarily interested in illumination levels, nevertheless have added to the knowledge of extraocular muscle fatigue. They set out to "(1) Determine the decrement in the amplitude of convergence reserve due to reading for an hour under levels of illumination of one and 100 foot candles, respectively, and (2) to investigate the direction of this effect after the cessation of the reading." They concluded that, "therefore, the assumption is made that muscular fatigue produced by reading, as indicated by changes in the tonicity of the internal recti muscles, is approximately three times as severe after reading one hour under one foot candle as it is after an hour's reading of the same printed matter under 100 foot candles."

The third group of ocular muscles, those controlling the pupil and the accommodation, known as the intrinsic muscles of the eye, have been

49. Sherrington, C. S.: The Integrative Action of the Nervous System, New York, Charles Scribner's Sons, 1906.

50. Duane, A.: Studies in Monocular and Binocular Accommodation with Their Clinical Application, Am. J. Ophth. **5**:865, 1922.

51. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1.

52. Howe, L.: Measurements of the Fatigue of the Ocular Muscles, J. A. M. A. **59**:1024 (Sept. 21) 1912.

53. Berens, C.; Hardy, L., and Pierce, H. F.: Studies in Ocular Fatigue: VI. Convergence Fatigue in Practice, Tr. Am. Ophth. Soc. **24**:262, 1926.

54. Luckiesh, M., and Moss, F. K.: The New Science of Seeing, Tr. Illum. Engin. Soc. **29**:641, 1934.

in the past and are continuously being studied in the laboratory. Failure of the pupil to react to a direct light stimulus and loss of the ability to accommodate normally are well known and useful signs for the diagnosis of general disease. In a study of the pupillary reactions Dr. Gifford and I [55] demonstrated the quantitive fatigue of these muscles. That general ocular fatigue or simple iridic muscle fatigue is shown by the change in size of the pupil during the course of a day's work is the conclusion arrived at by Luckiesh and Moss [56] in an experimental test.

The physiology of the function of accommodation is still not entirely understood, and much experimental work has been initiated without the achievement of entirely acceptable conclusions. Berens and his co-workers,[57] using Howe's ergograph, have studied the fatigability of this function. The inevitable presbyopia, or "old sight," which affects all persons past the age of 45 owing to gradual loss of accommodation, may be considered a sign of ciliary muscle fatigue. It is a common observation that the workman approaching this age period needs an additional lens to prevent fatigue due to close work.

COLORS

The subject of the color sense is entirely too stupendous to discuss in any detail in a paper of this type. Only a few of the more important phases which affect the worker in industry will be considered. In 1924 Parsons [58] wrote an entire volume on color vision. Since Sir Isaac Newton,[59] in 1704, showed that white light can be broken up into the primary spectral colors and these colors recombined to make white light, much work has been accomplished on the study of color mixtures. Helmholtz [60] in Germany and Maxwell [61] in England, whose labors have been continued by König [62] and Sir William Abney,[63] have indeed provided a basis of classics for continued studies. The occurrence of a congenital deficiency in the appreciation of color values had long been

55. Gifford, S. R., and Mayer, L. L.: The Clinical Use of the Sander Pupilloscope, Arch. Ophth. **6**:63 (July) 1931.

56. Luckiesh, M., and Moss, F. K.: Size of Pupil as a Possible Index of Ocular Fatigue, Am. J. Ophth. **16**:393, 1933.

57. Berens, C., and Stark, E. K.: Studies in Ocular Fatigue: III. Fatigue of Accommodation, Am. J. Ophth. **15**:216, 1932.

58. Parsons, J. H.: An Introduction to the Study of Color Vision, ed. 2, New York, The Macmillan Company, 1924.

59. Newton, I.: Opticks, London, W. & J. Innys, 1721.

60. Helmholtz, H. L. F.: Helmholtz's Treatise on Physiological Optics, translated from the third German edition, edited by J. P. C. Southall, Ithaca, N. Y., Optical Society of America, 1924, vol. 1.

61. Maxwell, J. C., cited by Parsons.[58]

62. König, cited by Duke-Elder.[51]

63. Abney, W. de W.: Researches in Colour Vision, Ztschr. f. Sinnesphysiol. **43**:70, 1908.

recognized, but it remained for John Dalton,[64] in 1798, to bring some practical ideas to the chaos then existing concerning this subject. More recently the question of color tolerance has been the subject of a symposium under the auspices of the American Psychological Association.[65] In addition to the testing of the color sense, a most unusual phase of this work has interested me. This is the question of color evaluation. In testing laboratory workers whose duty it was to match fluid color mixtures for end point determinations in chemical analysis, it was frequently found that two persons varied an exact amount in every deduction. I have been able to show that the evaluation in color matching may vary with different persons.[66] In his excellent treatise on colorimetry, A. C. Hardy[67] conveyed a clear understanding of the system adopted by the International Commission on Illumination in regard to the specific color of lights. In a more recent study of retinal fatigue by Bockoven and Wilcox[68] it was found that fatigue occurs first when the subject is viewing red; then in order come yellow, blue, white and green.

CONTRASTS

Perception of detail is greatly dependent on contrast. This fact has been recognized for centuries. It is as true in the perception of color as in that of black and white. In the simple test for visual acuity the ease of recognition of a letter or symbol is enhanced by the contrast of the black letter on the white background. It has come to be realized that in the evaluation of the visual field both for white and for colors the situation of the target in contrast to the amount of illumination of the perimeter arm is an essential factor. It is well understood that in advertising of various types, contrast in the makeup causes more persons to pause for a chance to see what the ad is all about. With such common examples in mind one may readily understand that the urge to investigate the phenomenon of contrast has been felt in many fields of endeavor. Similarly, it must be realized that certain types or degrees of contrast have an obnoxious effect on the mechanism of the eye or present a harsh affront to the cerebral appreciation of certain contrasts. Thus the esthetic sense of the subject must also be considered.

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64. Dalton, J.: Extraordinary Facts Relating to the Vision of Colours, Mem. Lit. & Phil. Soc. Manchester **28**:1, 1798.

65. The Inter-Society Color Council Symposium on Color Tolerance, Am. J. Psychol. **52**:383, 1939.

66. Mayer, L. L.: Use of the Fundus Colorimeter, Arch. Ophth. **12**:228 (Aug.) 1934.

67. Hardy, A. C.: Handbook of Colorimetry, Cambridge, Mass., Technology Press, 1936.

68. Bockoven, S., and Wilcox, B.: Significance of Retinal Fatigue in the Study of General and Nervous Disease, Arch. Ophth. **17**:1024 (June) 1937.

A practical view of contrast is illustrated by the work of Mitchell.[69] In considering the background light on a fine assembly process he found that a white or pale yellow contrast free from glare increased the output 19.5 per cent over that accomplished before contrast was considered.

ADEQUATE CARE OF THE EYES

Adequate care of the eyes in industry may be discussed from two viewpoints: the first, that of protection, especially in the hazardous occupations, and the second and not less important, that of general ocular care as it concerns health and efficiency. For example, J. J., aged 45, had been an expert machinist for fifteen years. His job was to regulate dials on electrical ammeters. For the past month complaints had been coming in to the company as to the accuracy of its ammeters. Only a certain number were questioned. A check-up showed that J. J. had been entrusted with the job on all the defective instruments. When questioned he acknowledged that his ability to see small print, figures and the dials had not been good of late, but he thought the light was poor. Examination of his eyes revealed beginning presbyopia and a need for glasses for close work. No further complaints about the ammeters were forthcoming.

The National Industrial Conference Board [70] has made the following statement concerning technicians and consultants:

1. Oculists—With the exception of surgeons, the consultants called in most frequently by industry are oculists. In industries in which keen vision is essential, they are sometimes employed on a part, or full-time basis. Consequently, oculists are found most often in companies manufacturing precision tools and electrical goods, and in the transportation, textile and machinery industries. Because it is customary in many establishments for the plant physician or nurse to test the visual acuity and color perception of employees at the time of routine physical examinations, oculists have been used more for treating eye injuries than for making eye examinations. When visual defects are discovered, employees are generally referred to oculists in the community for refraction or treatment. A few companies have optical surveys at regular intervals at which time an optometrist comes into the factory with his own equipment, tests the eyes of all employees, and fits them with glasses if necessary. In some instances the company pays for the glasses, and in others employees meet the costs but obtain a reduction from the local rates.

Some industrial physicians question the advisability of examinations other than by an oculist, because, while an optometrist may refract the eyes and prescribe indicated corrective lenses, he is not usually a physician and is therefore not so well qualified as an oculist to diagnose diseased conditions of constitutional origin. The correction of conditions so disclosed may require medical treatment rather

69. Mitchell, J. H.: The Relief of Eyestrain on a Fine Assembly Process, Human Factor **10**:341, 1936.

70. Medical and Health Programs in Industry, Studies in Personnel Policy, no. 17, National Industrial Conference Board, 1939.

than lenses. The American College of Surgeons, and the Conference Board of Physicians in Industry have gone on record as opposing the examination of eyes by other than qualified medical practitioners.

The importance of the medical ocular examination is stressed by Andrew [71] as follows:

Before taking up the medico-legal aspect I would like to amplify the suggestion previously made of the importance of a complete eye examination by an eye surgeon, before employing any worker, from the point of view of efficiency, accident prevention, and consideration of disability other than accident, as well as the avoidance of demands on the pension fund of the organization. The reasons for this examination are: First, to prove that he is physically competent to do the work; second, that any pathological conditions which may be progressive or which might be aggravated by minor injury or strain are not present, or if they are present, that they are a matter of record for consideration if their presence becomes a matter of importance in connection with a claim for compensation; and third, that the employee be given proper advice concerning any determinable tendency or inherent weakness so that he may take proper care of himself to avoid disability.

A complete examination of the eyes may easily be the most important part of a physical examination because it determines the employee's ability to see, which is likely to be a determining factor in his efficiency. Then again, such an examination may reveal conditions of the general health which are overlooked in an ordinary physical examination. For instance, unsuspected kidney disease, diabetes, brain tumor, syphilis and tuberculosis are often picked up by the ophthalmologist without the aid of a general physical examination.

I would stress also the importance of regular and systematic eye examinations, for the reason that the eyes change with advancing years, and because a man has good eyes at the time of the original examination is no criterion of what he may have in the succeeding years.

The Metropolitan Life Insurance Company [2] has this to say:

It is generally recognized that the examination of the eyes gives the most reliable evidence regarding senile nutrition and degenerations, and eye examinations should be included in the health examination. Although lenses may not always restore the original soundness of the eyes, they may be prescribed to prevent impairment of vision and further disease of the eye through eyestrain. The observation of pupil reactions, the testing of color and light perception, the mapping of the visual field, photography of the ocular movements, the determination of the tension of the eye-ball or the blood pressure within it, and X-ray examinations are all part of the complete eye examination.

The use by the oculist of drugs (cycloplegics) which temporarily paralyze the muscles of accommodation in the eyes, thus putting the eyes at rest during his tests, may cause groundless fears in those who do not understand the procedure. The drugs so used are called "drops" by the layman, because the solution of the drug is dropped into the eyes before examination. These drops, in the hands of a capable physician, are perfectly harmless and are used for the purpose of putting to rest the muscles of accommodation which by straining may be correcting or modifying an existing visual defect.

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71. Andrew, J. H.: The Eyes in Industry, Publication 205, National Society for the Prevention of Blindness, Inc., 1936.

Also, it must be remembered that glasses are prescribed for conditions other than poor vision. As an example, an individual with a short eye, to avoid a blurred image, compensates by using the small muscles within the eyes, a constant over-exertion which may result in the patient developing a headache. Since a headache is perhaps the most frequent single symptom of visual disturbances and also is common to so many ailments, a very careful examination of the eyes is required. Under such conditions it becomes necessary to put this muscle of the eye at rest by means of "drops" in order to search for the underlying ocular origin of the complaint.

Another very important point to consider is that frequently eye conditions develop from nose, throat and sinus diseases and permanent relief is possible only when the cause is removed. In such infections, any delay or attempt to remedy the condition with glasses may be serious to the patient.

While various modifications of methods of conducting eye examinations may be found in different industrial organizations, they conform essentially to one or another of the three following plans:

1. Eye examinations as part of the initial physical examination given to all applicants for employment. This usually consists of a superficial eye test in which the applicant is asked to read with each eye the indicated lines on the Snellen chart, and notation is made also of any gross defects of the lids or eyeballs. This examination is made by the doctor or nurse for the purpose of either rejecting the applicant or deferring his employment until he has his vision corrected at his own expense, to meet the requirements of the job.

2. Initial and periodical eye examinations, including refraction and prescription for glasses when indicated, of all employees. These are made by a competent oculist who arranges either to conduct the examinations at the plant or to have groups of employees referred at stated hours to his office.

3. Constant supervision of visual defects of employees. A full time oculist is employed as a member of the plant medical staff and is provided with the space and facilities for treating all eye conditions contracted or acquired among the employees.

Crude selection of those who need glasses consumes not more than ten or fifteen minutes. About half an hour of the oculist's time is required to determine the defect and measure for glasses in each case. After the glasses are supplied, the employee returns for a second brief visit to the oculist to have his sight tested with the glasses to make sure that it has been properly corrected.

The four prime factors in conserving vision as noted by Slyfield,[72] ophthalmologist for the Duluth, Missabe & Northern Railway Co., are (1) periodical visual examinations, (2) protection of the eyes, (3) enforcement of safety rules and (4) skilled treatment of injuries to the eyes. Bedell [73] gave the answer as follows:

At our final meeting it fell to my lot to open the discussion, which was summarized under three headings.

1. Eyes cannot be comfortable unless correct glasses are worn in their proper position. The lens focus must be for the work at hand. For instance, a 50 year old architect working on the board 20 inches from the eyes would need entirely

72. Slyfield, F. F.: Conserving Eyesight, Nat. Safety News **39**:201, 1937.
73. Bedell, A. J.: Eyes and the Office Worker, Hygeia **16**:210, 1938.

different glasses than he did for the same work at relatively the same position when he was 20 years old.

2. The general health of the employee must be maintained at the highest level. A chronic debilitating disease necessarily reduces the worker's efficiency.

3. Experiments have proved that for close critical work the illumination must be more uniform and better dispersed than that which we formerly considered adequate and that both shadow and glare must be avoided. How this is to be accomplished depends on the type of work, the size of the room and the number of workers in the room.

Kuhn,[74] in a report based on the examination of 16,332 employees, reported that "no scientific evaluations of methods of visual testing of employees in industry, such as have been made in the schools, are available." She also found that "medical guidance, supervision and control with the cooperation of management are absolutely essential in a field (ophthalmology) so liable to commercial exploitation." In his report of a survey of 15,000 employees, Rainey [7] concluded that "because the visual efficiency rapidly decreases with age, due to the loss of accommodation and the prevalence of subnormal and abnormal conditions of the eyes, *the need for periodic visual-efficiency examinations at one- to two-year intervals is apparent.*" (The italics are mine.) Adequate care of the eyes was summarized by Davidson [75] as follows:

1. The arguments for eye examination of industrial employees are derived from four fundamentally different motives: safety; medico-legal problems in workmen's compensation; industrial selection; and vocational guidance. The first two arguments are in the domain of public concern and public health—the last two are in the interest of industry and of the worker respectively.

2. Contrary to prevalent conceptions, the problems involved concern only about 4 to 6 per cent of the working population, and the term, "defective vision," as applied to them, is too broad. It should be specific as to the different elements in vision—visual acuity, color vision, light sense, indirect vision and depth perception, and their varying importance from the different angles of approach.

3. The main problems are safety and compensation for eye injuries. The former is partly solved by the State-controlled examination of all transport employees; by railway, marine, aviation and motor vehicle licensing provisions; and its standards are being now established by an international congress. There should be a pre-employment examination by State agencies for both purposes, at intervals of three to five years.

4. For industrial selection, vocational guidance and elimination of occupational diseases, a different procedure in standardization, on the basis of the special requirements for types of occupation, should be worked out, and should be the task of annual periodic eye examinations by plant medical services.

5. Eye examinations for the purposes mentioned should be the work of ophthalmologists, or "eye physicians," exclusively.

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74. Kuhn, H. S.: An Appraisal of Visual Defects in Industry, Based on a Study of 16,332 Cases, Tr. Am. Acad. Ophth. (1940) **45**:208, 1941.

75. Davidson, M.: Examination of the Eyes of Industrial Employees—Why and How? Sight-Saving Rev. **3**:38, 1933.

Adequate care in industry by the general physician necessitates use of the services of a specialist in ophthalmic work, for the general practitioner, as he will readily acknowledge, is not equipped to give expert care of the eyes. Resnick and Carris [76] gave as the basis for adequate care of the eyes the following assumptions:

> First, the elimination of eye hazards in industry is not only a moral obligation, but a good business proposition. Second, goggles at best are a handicap; the first effort, therefore, should be directed toward elimination of the hazard itself by revising the process of manufacture, by redesigning the machine or tool at the point of operation. Third, few people have normal vision; greater attention should, therefore, be given to examination of the eyes of employes, to consideration of the condition of the eyes with relation to the visual requirements of the job, and finally to the correction of defective vision and the treatment of eye diseases and eye infections among employes.

These authors went on:

> It is recommended that the eyes of all applicants for employment be examined and that the correction of refractive errors be made a condition of employment, but that the employer exert every possible means compatible with good business to enable the employe to secure glasses at a moderate cost and, when necessary, by paying for them on the installment plan. The eyes of present employes also should be examined at least once every two years. It is particularly important that the eyes of men and women who are engaged in close or exacting work be carefully examined on employment and periodically thereafter.
>
> It is urged that the condition of the eyes of employes—even where vision has been corrected by glasses—and the visual requirements of the particular work that the employe is to do be considered in assigning each worker to his job. The International Harvester Company does this through Job Specification cards which are placed in the hands of the medical and employment departments. A card for each worker in his department is also given each foreman. The works doctor, the employment clerk or manager, and the foreman, each know that a person engaged for any particular job must meet certain physical requirements; if the medical examination or subsequent observations by either the works doctor or the foreman show an employe unfit for certain work because of the condition of his eyes or indicate that the condition of his eyes in combination with the visual requirements of the job predispose him to accident or to serious impairment of vision, he is returned to the employment department for transfer to other work.
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> "This," writes a representative of the Industrial Relations Department of this company, "is, in my opinion, the biggest contribution that we have made recently to the prevention of blindness and accident involving other injuries.

To summarize, the following measures appear necessary to adequate care of the eyes in industry: (1) periodic tests for vision and color by competent ophthalmologists, (2) a lighting survey, (3) safety measures against eye hazards, (4) cooperation of industrial personnel and medical advisers and (5) competent medical attention in the case of accidents to eyes.

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76. Resnick, L., and Carris, L. H.: Eye Hazards in Industrial Occupations, National Society for the Prevention of Blindness, Inc., 1924.

OCULAR EXAMINATIONS AND MEDICAL CARE

Since the time of Helmholtz,[77] who invented the ophthalmoscope, the physician has been equipped with an instrument by means of which the actual changes in the tissues of the body may be seen. Blood vessels are magnified from fifteen to forty-five times with the modified instruments devised by May,[78] Gullstrand[79] and Friedenwald.[80] A general disease affects all portions of the body. Thus, examination of the fundus of the eye may reveal a disease condition long before one is able to recognize it in any other part of the body. The importance and the advantage of this fact in the general care and health of the industrial worker cannot be overemphasized. In addition, the eye contains elements originating from the three tissue layers of the body, the surface ectoderm, the mesoderm and the neural ectoderm of the embryo. The eyelids and the cornea are involved in many cutaneous diseases. The acute infectious diseases, such as measles, scarlet fever and pneumonia, may involve the ocular structures through the blood vessels. Syphilis and tuberculosis are often first manifested by changes in the ocular structures. Disorders of metabolism and of the endocrine glands, such as gout, diabetes and hyperthyroidism, frequently have ocular signs. Changes in the nervous system in which so important a fiber from the brain as the optic nerve may be involved leave no doubt as to the necessity of adequate ocular care. No statistics are available, but it is generally conceded that a certain percentage of persons are born with only one good, seeing eye. Others come to this status during childhood owing to disease or injury. Thus a group of workers not only are handicapped as to their efficiency—having no binocular single vision and depth perception and being unable to see things approaching from one side—but in addition need adequate care of the remaining eye. That both industries and compensation boards are cognizant of this fact will be shown later. In many hospitals it is routine practice to examine the eyes, especially the retinal background, of every patient admitted for general medical care.

A standard ocular examination for employees in industry is slowly being evolved. The examinations have varied according to the type of work done by the employee and the interest expressed by the employer and the personnel director. Certain companies require an ocular

77. Helmholtz, H. L. F.: The Description of an Ophthalmoscope, translated by T. H. Shasted, Chicago, Cleveland Press, 1916.

78. May, C., cited by Bell, W. O.: Recent Advances in the Construction of the Ophthalmoscope, Arch. Ophth. **7**:601 (April) 1932.

79. Gullstrand, cited by Langdon, H. M.: The Electric Ophthalmoscope, Am. J. Ophth. **8**:740, 1925.

80. Friedenwald, J. C. A.: Critical Study of the Modern Ophthalmoscope: Contributions to Its Construction and Use, Tr. Am. Acad. Ophth. **26**:381, 1928.

examination before employment; among these are Sears Roebuck and Company, Montgomery Ward and Company, General Motors Corporation, Bausch and Lomb Optical Company, the Pullman Company and the Metropolitan Life Insurance Company. Many of the firms have a permanent industrial ophthalmic clinic with an oculist in charge on a full or a part time basis. The eyesight survey has come to be a necessary adjunct to the complete efficiency of the worker in many plants. A word of caution must be said at this point concerning such surveys. A great number of optical concerns in order to increase their business will go through a plant with no expense to the management to check vision and to make glasses. For a time this was the only service available and certainly was better than no examinations. However, for some ten years ophthalmologists throughout the country, among them myself, have been able to offer a valuable substitute. This is a survey by a trained ophthalmic physician and surgeon who is totally uninterested in the sale of glasses. Arrangements are made entirely by the plant management with some first class optical concern for the making of glasses at a reduced rate because of the number needed. Vogel,[81] of New York city, has reported on some of his work. Kuhn's [74] recent study of 16,332 persons in the steel-producing district near Chicago is an outstanding report of such work. Rainey [7] has also given an account of such a survey and of its ultimate value.

Aside from the aforementioned reports, a search of the literature reveals little of a completed nature in this field. Many oculists, however, are doing such work and have not taken time to put in writing the results of their studies. I have had many contacts with such physicians, the value of whose work along survey lines from year to year is attested by letters from employers, personnel directors and the employees themselves.

Without going into too much detail, I may say that authorities on such surveys agree that the following procedures should be included: (1) examination of each eye separately for visual acuity, (2) testing of the visual acuity of each eye separately with correcting glasses, (3) measurement of stereopsis, (4) testing for color deficiencies, (5) measurement of muscle balance, (6) examination of external portions of the eyes, (7) ophthalmoscopic examination, (8) testing for adequate illumination, (9) surveying for hazards and (10) making of recommendations for protective goggles and other equipment.

PREVENTION OF AND PROTECTION AGAINST HAZARDS

The prevention in industry of injuries in general and of ocular injuries in particular has been a crusade of the times. There is no

81. Vogel, M. A.: Eyesight Surveys, Personnel J. **16**:22, 1937.

dearth of literature on both general and ocular protection. Even on the latter volumes have been written, and it must be the purpose of this section to cite the high spots and leave it to the reader to seek out the details. Of paramount importance is the fact that, in spite of the ability of science to develop artificial hands, arms and legs, no one has produced an artificial eye that can see. Resnick and Carris [76] answered the question "What, in a nutshell, are the eye hazards of industry?" in this way:

> Foremost, of course, are the accident hazards: flying chips of metal, mineral, or wood; splashing liquids—molten metal, acids, or other injurious chemicals; and explosions of endless variety. Then there are the hazards of infection and of eye diseases: through neglect of eye injuries; through contact with carriers of contagious disease; and through exposure to excessive radiated heat. Finally there is eye strain resulting from improper or inadequate lighting; from improper vocational placement; from ignorance of, or disregard for, the existence of defective vision.

It has been stated that there are close to 8,000 persons who have been blinded by the eye hazards of industrial occupations and more than 80,000 persons who have lost the sight of one eye as a result of these hazards.[82] The cost has been estimated at more than $100,000,000 a year, and more startling is the statement that 98 per cent of visual loss is needless.[83]

The following protective technics have been recommended:[84] (1) control of toxic materials, gases, dusts and vapors; (2) use of protective goggles against flying objects and radiant energy, and (3) provision of adequate and suitable illumination.

Such measures not only protect the eyes of workers but reduce to a minimum the chances of claims by malingerers, since would-be malingerers, because of the psychologic effect, are wary of them.

The volume by Resnick and Carris [76] is indeed a fertile source of information on eye hazards in industry and should be in the armamentarium of all agencies interested in the eye and in industry. The point of view is expressed by the excerpts previously quoted.

The United States Department of Commerce in 1938 issued its "American Standard Safety Code for the Protection of the Head, Eyes, and Respiratory Organs." In this pamphlet the specifications for lenses,

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82. Resnick, L.: The Cost of Eye Hazards in Industry, in Protecting Eyes in Industry, Bulletin 37, United States Department of Labor, Labor Standards Division, 1940.

83. Carris, L. H.: Eyes Saved in Industry, Eye, Ear, Nose & Throat Monthly **9**:343, 1930; reprinted, Publication 62, Natioanl Society for the Prevention of Blindness, Inc., 1930.

83. Greenburg, L.: Vision and Eye Protection: A Symposium, Publication 299, National Society for the Prevention of Blindness, 1939.

protective goggles, masks, etc., for all types of work are given in detail. Coblentz and Stair,[85] of the same department, have studied the spectral transmissive properties of colored eye-protective glasses, Guilbert's paper,[86] with its startling title, "No One Enters This Plant Without Goggles," emphasized the profits obtained on a small initial investment. The National Society for the Prevention of Blindness has published the experiences of five hundred and eighty-three companies in the saving of eyes in industry. In the foreword the late Park Lewis said:

> Despite the splendid accomplishments of many individual firms in the prevention of accidents in general, and specifically in the prevention of eye accidents, such accidents are still considered by many persons inherent or unavoidable accomplishments of certain industrial processes. Despite the tremendous financial savings through accident prevention publicity and authentically reported by some of the leading industrial concerns of America, there are still thousands of employers who regard as an unavoidable (though evil) necessity the payment of thousands of dollars for the destruction or injury of the eyes of their employees. That these are misconceptions, that industrial eye injuries are largely preventable and that their prevention is productive of enormous savings to employer, employee and the nation, are convincingly demonstrated in the findings of this study and the interpretation of their significance.

Table 1 in this pamphlet shows how 4,654 eyes were saved in two years in five hundred and eighty-three plants where 578,396 employees were at work. Recently Allen and Carman,[87] as part of a symposium before the Third Annual Congress on Industrial Health, thoroughly discussed the protective equipment for eyes in industry. They stressed the importance of accident prevention by the greatest cooperation of all parties concerned. They also brought out the point that in the smaller factory or shop, where the expense of financing is a large item, there is more chance that adequate preventive measures will be neglected. Sappington[88] has shown how the industrial physician and the safety engineer may find means of cooperating in saving sight. When management is shown the value of hazard prevention by statistics which demonstrate actual savings in dollars and cents there is no longer any difficulty in putting over the idea of protecting the eyes and preventing hazards.

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85. Coblentz, W. W., and Stair, R.: Spectral-Transmissive Properties and Use of Colored Eye-Protective Glasses, Circular C 421, United States Department of Commerce, Bureau of Standards.

86. Guilbert, H.: No One Enters This Plant Without Goggles, Factory Management & Maintenance, March 1938.

87. Allen, T. D., and Carman, H. F.: Protective Equipment for Eyes in Industry, J. A. M. A. **116**:1343 (March 29) 1941.

88. Sappington, C. O.: The Co-Operation of the Physician and the Safety Engineer in Saving Sight, Sight-Saving Rev. **5**:16, 1935.

WORKMEN'S COMPENSATION LAWS

Sherman [89] stated that the first employer's liability laws were enacted by a few states some thirty years ago. The history of this type of statute makes interesting reading; space does not permit of its elucidation at this point, but a source will be mentioned later. In 1900 Hansell [90] wrote of the estimation of the amount of injury caused by visual loss. In 1901 and 1902 Würdemann [91] studied the economic limitations of visual acuity and later,[92] in his book on injuries of the eye, gave much attention to the legal phase. Shastid [93] wrote of ophthalmic jurisprudence, and the work was later included in the American Encyclopedia of Ophthalmology. Chapman [94] and Sharp [95] wrote of loss of industrial vision. Allport [96] seems to have been the first in this country to discuss the workmen's compensation laws in regard to loss of vision. Smith [97] in 1921 made estimates on compensation, and in 1925 the Committee on Compensation for Eye Injuries of the American Medical Association made its report.[98] This has recently been revised.[99] In 1928 McAuliff [100] called attention to the fact that the defects in 20 per cent of workers existed before employment and therefore were not compensable. It remained for Snell,[101] in a recent all-inclusive volume, to sum up existing ideas. He found that every state but one has a workmen's compensation law and that these differ from state to state. Direct quotations from

89. Sherman, E. S.: The Management of Industrial Eye Injuries in Their Relation to the Workmen's Compensation Laws, Sight-Saving Rev. **6**:56, 1936.

90. Hansell, H. F.: Estimation of the Amount of Injury to the Business Capacity of the Individual from Partial or Complete Loss of Vision, Ann. Ophth. **10**: 605, 1900.

91. Würdemann, H. V.: The Economic Limitations of the Visual Acuity in Various Trades and Professions, J. A. M. A. **38**:380 (Feb. 8) 1902.

92. Würdemann, H. V.: Injuries of the Eye, ed. 2, St. Louis, C. V. Mosby Company, 1932.

93. Shastid, T. H.: Ophthalmic Jurisprudence, Chicago, Cleveland Press, 1916.

94. Chapman, N. A.: Indemnities Following Injuries to Eye: How Shall We Determine Them? Wisconsin M. J. **17**:54, 1918.

95. Sharp, W. N.: Loss of Industrial Vision, Am. J. Ophth. **3**:434, 1920.

96. Allport, F., Jr.: Workmen's Compensation with Especial Reference to Loss of Vision, J. A. M. A. **74**:166 (Jan. 17) 1920.

97. Smith, E. T.: The Estimation of Compensation in Disability Resulting from Accidental Loss of Visual Acuity, Tr. Am. Ophth. Soc. **19**:149, 1921.

98. Cited by Snell.[101]

99. Presessional Bulletin, Section on Ophthalmology, American Medical Association, 1941, p. 7.

100. McAuliff, cited by Snell.[101]

101. Snell, A. C.: A Treatise on Medicolegal Ophthalmology, St. Louis, C. V. Mosby Company, 1940.

Snell's book sum up so adequately the various phases of this subject that no excuse seems necessary for their use. He said:

> In spite of these differences, compensation laws have succeeded in assuring compensation of some sort to the worker and in reducing the cost and difficulties of collection. These laws have simplified court procedure and the legal issues involved. They have also reduced the number of accidents. . . . In so far as injuries to the eyes are concerned, the fault in the present laws lies in the lack of uniformity among the different states in determining the degree of visual impairment, or the percentage loss of use, for partial permanent disabilities. On the whole, however, these laws to protect workers are a decided advance in social economics over older methods, and are entirely justified in consideration of the many hazards involved in this industrial age.

Frequently the compensation law makes a difficulty for the practicing physician, especially if he is not in the habit of doing industrial work on a reduced fee basis. A private patient may seek the advice and care of the oculist after an accident without knowing that he comes under the law. Subsequently, when the usual statement for such service is received, the bill is turned over to the insurer, who questions the seemingly excessive fee. Such cases are often brought before a board or judge for the compensation commission, taking valuable time from the physician and giving him no compensation therefor whether or not the court decides in his favor.

Snell drew the following general conclusions:

> The compensation statutes in general provide an adequate basis for computing visual disability although they lack uniformity and they lack definiteness. However, there are striking inequalities in the amounts of compensation for identical degrees of visual disability, because the methods used for computing visual disability, both those provided by statute and those established by administrative law, differ widely among the states. Moreover the mathematical provision that permanent partial disability shall be computed on the basis of proportionate loss of useful vision is often ignored or misinterpreted by those responsible for determining the degree of such disability. It would seem obvious that the compensation statutes of all the states, in fairness to all parties concerned, should contain definite uniform provisions which in understandable language should cover all classes of visual disability; and that for permanent partial disability these statutes should set forth clearly a method of computation having a scientific basis.

Snell expressed the opinion that the following faults are to be found in the existing compensation laws:

> (1) The failure to comprehend the meaning of the test for visual acuity; (2) the failure to define the use of such ambiguous terms as "loss of an eye" or "loss of use of an eye"; (3) failure to provide for the determination of a percentage loss of use when statutes provide that awards shall be made on the basis of a proportionate loss; (4) failure to comprehend the importance of, and the necessity for, the use of correcting lenses to correct refractive errors; (5) the failure to recognize and to give due consideration to visual defects existing prior to industrial injury.

It is interesting to note that, although preemployment examinations have been stressed for many years, self insurers have insisted on these, while the insurance companies, because their budgets are set for months in advance, are not interested in protecting their insured employees, the companies insured or themselves.

Frequently it is difficult for the ophthmalogist to decide whether or not a lesion of the eye existed before injury and testimony by either side may be given for or against its having done so, thus confusing the compensation commission, judge or jury.

INSURANCE CARRIERS AND SELF-INSURERS

There is a growing tendency for large firms to become their own insurers, setting aside certain funds which take care of employees' risks and breed good will, since a disinterested party is not drawn into the picture. At the same time, the firms have discovered that they actually save money. The usual procedure is to insure against large claims for personal neglect and similar suits. In addition, the physician employed is either paid a retainer's fee or receives adequate compensation in fees for each employee treated. The physician becomes interested in hazard prevention and proper illumination and also becomes the adviser for the employee and his family. For example, Sears Roebuck and Company keep files on each employee, and these contain copies of advice and prescriptions from the employee's private physician, who is eager to cooperate with a firm that is personally interested in each employee. The physician for an insurance company as a rule works under pressure because of the low fee he receives for each visit of the employee, and in addition he has a tendency to become callous, impersonal and careless. This reflects on the honest, careful oculist and decreases respect for the physician in general. The employee loses much when such difficulties are met with, since he may obtain inferior medical service and may be kept longer away from his job. Further comment on this aspect of industrial ophthalmology makes itself obvious.

FREE AND PART PAY OPHTHALMIC CLINICS

In larger communities many employees of the smaller firms, which do not have medical care available, seek aid and advice from clinics. Analyses have shown that as a rule working people do not take advantage of such services to the extent that they are entitled because of their low earning capacity. These clinics as a rule are run on a high level, and expert care is given. There has been a tendency in some clinics of late years not to admit accident victims who may be subject to workmen's compensation laws. Davidson [102] reported that New York

102. Davidson, M.: The State Labor Department Ophthalmologist, Indust. Med. **8**:43, 1939.

is the only state in which two full time ophthalmologists are attached to the labor department for the purpose of examining claimants for compensation for ocular injuries. The patient entering a clinic after an injury to the eye for which hospitalization is necessary is usually asked to choose from the hospital staff a physician who will treat him as a private patient from whom payment may be expected. Also, it must be remembered that the majority of clinics and hospitals are not prepared to examine patients with ocular injuries and report on them in the manner required by the various compensation boards. Thus it is readily seen that the free and part pay clinics are not efficient at examining patients with industrial ocular injuries.

TYPES OF OCULAR SERVICE FOR INDUSTRY

What of the ocular service for industry? Must this be left to the optical survey, to the general practitioner alone or in cooperation with a consulting specialist, to the factory first aid station or to the factory hospital? Finally, what has the ophthalmologist to offer? It may be realized from the trend of thought in the previous pages that it is my belief that the problem ultimately will be dumped in the lap of the ophthalmologist. And now what of past experience?

First, I have spoken of the optical survey, which is held to be totally inadequate. Second, the ophthalmic clinic is becoming less and less available. Third, the first aid station, especially in smaller plants, where a nurse may or may not be in attendance, provides no real means of proper care. Certain large industrial concerns find it profitable because of the type of work and hazards to employ a full or a part time ophthalmologist. The setups in these organizations are the most adequate. Among these firms are the Pullman Company, R. K. LeBlond Machine Tool Company, Bausch and Lomb Optical Company and the Metropolitan Life Insurance Company. Reports from many of them attest in statistics the high value of such a service both to the employee and to the management.

The following procedure, which I have used for many years in numerous concerns, has given satisfaction.

A preliminary survey made at the plant allows about ten minutes to each employee. The examination consists of: (1) ascertaining the name, age and type of work; (2) testing the visual acuity of each eye separately and together for distance; (3) testing the visual acuity of each eye separately and together for near work; (4) neutralizing the glasses worn and testing the visual acuity with them; (5) cursorily examining each eye externally; (6) examining with the ophthalmoscope each eye with the pupil undilated; (7) testing the color vision, and (8) making a photometer record of the illumination in the plant.

A moderate fee may be charged for the time consumed in making such a survey, this to be paid by the management alone, by the management and the

employees or by the employees alone. The first method is the usual one. After a thorough study of the records a report is sent to the personnel director embodying the following points:

1. The following employees need no office examination at present.

2. The following employees will not be examined in the office unless they have ocular complaints or headaches.

3. An office examination is recommended for the following employees in six months' time.

4. An office examination is recommended for the following employees in a year's time.

5. The following employees are to be seen at the office either because they were not seen at the plant or for a check of a previous office visit.

6. The following employees need office attention because of a diseased condition of the eyes.

7. The following employees need an office examination at present because of poor vision, headaches, need of a change of glasses, etc.

8. The following employees are color blind.

9. Protective goggles are recommended for the following employees.

10. An increase in illumination is recommended as follows.

With these recommendations are given the employee's name, his visual acuity and his visual efficiency percentage. A fee commensurate with the earning ability of the employee is paid for the office visit, and after this visit a further report is made to the personnel director to keep the record in shape. With such a setup a close contact between management, employee and ophthalmologist is established, hazards and illumination are adequately and efficiently cared for and the ophthalmologist has fulfilled a real need in industry.

It is interesting to note at this point the requirements for a rating in ophthalmology recently outlined by the Workmen's Compensation Committee of the Medical Society of the State of New York:[103]

1. A candidate for qualification in the field of ophthalmology shall present a license to practice medicine in the State of New York, and evidence of registration for the current year with the Department of Education.

2. The candidate shall be of high ethical and moral standing in the profession.

3. The Committee may require letters of recommendation from outstanding physicians and specialists in the field of ophthalmology in support of the above and as evidence of professional standing.

4. The applicant shall present evidence of a regular internship of from one to three years in a duly accredited hospital and shall also present evidence of a residency in the specialty of ophthalmology covering a period of from one to three years, in an institution recognized as qualified to teach residents in this specialty or the equivalent of this training.

5. Subsequent to the completion of a residency, the physician shall have had experience in private practice, and in hospital or clinical affiliations, for a period of at least one year; this being dependent on the length of training in the specialty during internship and residency. Where the period of residency has been two to

103. Murphy, H. J.: Registration of Physicians, Indust. Med. **10**:200, 1941.

three years, the minimum period of private practice may be accepted. Where the residency has been of but one year following internship, a minimum of at least three years of subsequent training in the specialty shall be required. Physicians who have been in practice for ten years or more and have not had a period of residency in the specialty but have been appointed to positions on the attending staff of a reputable and accredited hospital in the specialty may be qualified provided they can produce satisfactory evidence of independent ophthalmological (surgical) work during this period of hospital association.

6. In the case of reputable well-known specialists of outstanding ability any or all of the above standards may be waived by the Committee.

7. The diploma of the American Board of Ophthalmology may be accepted in lieu of evidence of internship and residency provided, however, the possessor of such diploma shall have had at least one year of experience in private practice. In the case of physicians trained in foreign countries who are not of outstanding ability and reputation or whose credentials may be difficult to substantiate, the Committee should require evidence of association with an accredited institution in this country for a period of at least one to three years together with letters of recommendation from local specialists connected with such institution and known to the Committee.

Items 8, 9, 10 and 11 refer to the designation of the specialists.

ILLUMINATION STANDARDS AND METHODS

Hardy [20] in 1932 discussed illumination and eyesight in industry before the Greater New York Safety Conference. He stated that less than 25 per cent of 50,000,000 incandescent lamps installed in industry were equipped to prevent glare. He listed the defects of illumination as relating to (1) intensity, or quantity; (2) quality, or spectral composition; (3) distribution; (4) steadiness; (5) diffusion, and (6) direction. He recommended "an illumination survey of the plant or factory by an illuminating engineer in conference with the plant physician or ophthalmologist." If this is impractical an interested person armed with a copy of the American Standards code of lighting and a cheap foot candle meter will be able to give a good account of the conditions.

In addition to the advice given by Hardy, the laboratory contributions cited in a previous portion of the paper add much from the theoretic side. From a practical standpoint it is necessary that at least 10 foot candles of light fall on the working surface in such a way that no glare is produced from the surface or from any point at the level of the eyes. When a shiny surface is being worked on a pair of polaroid glasses will afford ample protection. Illuminating engineers are eager and willing to cooperate and should be called on for advice.

2007 Wilshire Boulevard.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

PASSAGE OF HORSE SERUM FROM THE BLOOD STREAM INTO THE AQUEOUS HUMOR OF NORMAL AND IMMUNIZED ANIMALS. L. GUY, Am. J. Ophth. **23:** 1209 (Nov.) 1940.

From his investigations Guy presents the following summary and conclusions:

"1. In normal rabbits, 5.0 cc. of whole horse serum injected intravenously were necessary to produce sufficient concentration in the circulating blood to cause horse serum to pass into the aqueous within an interval of five hours.

"2. In rabbits in which the anterior chamber of an eye had been injected with horse serum, a much smaller quantity (2.0 c.c.) of horse serum injected intravenously produced a concentration in the circulating blood sufficient to cause its penetration into the aqueous.

"3. In rabbits immunized with horse serum, a smaller amount of intravenously injected horse serum passed from the blood stream into the aqueous than was the case in normal rabbits.

"4. When rabbits, immunized with horse serum and having anti-horse-serum precipitins in the blood stream, received an injection of horse serum into the anterior chamber, there was greater penetration into the aqueous following intravenous injection of horse serum than in animals with no immunization otherwise similarly treated.

"5. After injection of horse serum into one eye, intravenous administration of horse serum caused penetration of the antigen into the contralateral eye but in less quantity than that which penetrated into the previously injected eye."

W. S. REESE.

Conjunctiva

GONOCCOCCIC CONJUNCTIVITIS IN CHILDREN. L. K. SWEET, J. Pediat. **19:** 1 (July) 1941.

Sweet treated 59 patients having gonorrheal conjunctivitis with sulfanilamide, sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) or both. Three patients (respectively 10 years, 3 days and 2 days old) were treated with sulfathiazole (2-[paraaminobenzenesulfonamido]-pyridine). In each instance the ocular condition improved remarkably within twenty-four hours after therapy was begun. Smears free from gonococci were obtained from the ocular discharges after one, six and three days, respectively. There were no toxic manifestations, and there were no bacterial complications. Of 30 patients treated with sulfanilamide the smears of 24 were negative for gonococci within one to six days after therapy. Thirty-three patients, including the 4 who failed to

respond to sulfanilamide, received sulfapyridine, and 31 of them recovered within from one to twelve days. Among these 31 were 3 of the patients who had not responded to sulfanilamide. Only one corneal ulcer developed; this was in a patient receiving sulfanilamide. Reports on more than 45 patients with gonorrheal conjunctivitis treated with sulfapyridine collected from the literature show the results to be comparable to those obtained by the author.

J. A. M. A. (W. ZENTMAYER).

Congenital Anomalies

CLINICAL AND HISTOLOGIC OBSERVATIONS IN MELANOSIS BULBI CONGENITA: REPORT OF TEN CASES. H. BRONS, Klin. Monatsbl. f. Augenh. **105:** 55 (July) 1940.

Ten patients with melanosis of the eyeball were examined for the purpose of determining a possible relation to a malignant process. The melanosis was discovered at birth in all but 2; it was noticed in one of these one year after birth and in the other at the age of 21. Brons thinks, nevertheless, that a congenital inclination existed in all the patients. Only one eye of each patient was melanotic. The hair and the iris of all except 1 were dark brown. No functional difference existed between the melanotic and the normal eye. The sclera, iris and choroid were involved in every patient, the conjunctiva in 7 and the disk in 1. Symptoms such as asymmetry of the face and telangiectasias of the blood vessels of the face and neck, always on the same side as the melanosis, were observed. One patient had several nevi on the face.

In 1 patient with congenital melanosis a sarcoma of the choroid developed in the melanotic eye. The larger portion of the tumor was unpigmented. A connection between melanosis and sarcoma could not be established in this patient, nor was it possible to prove a transition of melanosis to a malignant process in any of the 10 patients. The author describes several forms of "warty" iris observed. A number of pictures, some of them colored, illustrate the article. K. L. STOLL.

Cornea and Sclera

A NOTE ON THE TREATMENT OF THE SEQUELAE OF PERFORATED CORNEAL ULCER. P. C. KRONFELD, Am. J. Ophth. **23:** 1014 (Sept.) 1940.

Kronfeld gives an interesting account of the particular surgical problems found in China, where there are an unusual number of perforating corneal ulcers and resulting anterior synechiae. He discusses the surgical measures necessary immediately after corneal perforation and those for use when the iris has healed in the corneal wound.

W. S. REESE.

STUDIES ON KERATOCONUS RELATIVE TO THE EFFECT OF PROLONGED APPLICATION OF PRESSURE. T. L. TERRY and J. F. CHISHOLM, Am. J. Ophth. **23:** 1089 (Oct.) 1940.

In this rather comprehensive article Terry and Chisholm consider the development and growth of the cornea, its tensile strength and the

history, occurrence, etiology and pathology of conical cornea. Treatment with a pressure bandage was successful, the success being attributed to a reaction of fibrous tissue growth or to the normal tendency of the cornea and the sclera to contract and thicken when intraocular pressure is lowered indirectly by great elevation of the extraocular pressure.

W. S. REESE.

A SURVEY OF SUPERFICIAL PUNCTATE KERATITIS IN TASMANIA WITH THE RECORD OF A MILD EPIDEMIC. J. B. HAMILTON, Brit. J. Ophth. **25:** 1 (Jan.) 1941.

In the mild epidemic reported there were 92 cases, a case incidence of 1.38 per cent. Of the patients, 45.65 per cent were male. The highest incidence among male patients was in the third decade and among female patients in the fifth and sixth decades. The city incidence was 1 in 1,000 and the country incidence 1 in 1,750. No seasonal variation was noted, but the disease was often accompanied by infection of the respiratory tract as has been frequently noted. No immunity was acquired. The disease did not appear to be infectious. In 25 cases both eyes were involved.

Marginal keratitis, corneal ulceration, disciform keratitis, dendritic ulceration, phlyctens, folds in Descemet's membrane, hordeolum, herpes facialis and probably warts occurred as complications.

Since the institution of painting of the palpebral conjunctiva with 2 per cent silver nitrate solution the prognosis is that the eye will return to normal within a fortnight; the actual duration of the treatment has been seven and three-tenths days.

The article contains a review of the literature, with the views of the contributor.

W. ZENTMAYER.

General Diseases

RETINAL LESIONS IN LUPUS ERYTHEMATOSUS. A. E. MAUMENEE, Am. J. Ophth. **23:** 971 (Sept.) 1940.

Maumenee remarks on the frequency of retinal or choroidal lesions in cases of acute lupus erythematosus disseminata, a disease characterized by low grade fever, endocarditis, nephritis, erythematous lesions, leukopenia and anemia. He reports 5 cases and gives the following summary:

"1. The case histories including postmortem examination of four patients with acute and one patient with chronic lupus erythematosus disseminata are presented. Ophthalmoscopic and histological findings in the eyes of these five patients consisted of: (a) cytoid bodies of the retina, with an ophthalmoscopic appearance of small fluffy-white areas. These areas developed in all cases before death. (b) Small superficial retinal hemorrhages, noted ophthalmoscopically in three cases, and only twice in histological studies. (c) Slight papilledema, diagnosed in three cases before death, but demonstrable in only two cases in histological preparations. (d) Slight round-cell infiltration of the choroid, 'septic choroiditis.' This type of choroiditis could be seen histologically in all cases. (e) Choroidal exudates and hemorrhages, found on histological examination in one case.

"2. The cytoid bodies found in the retinae of these five patients on both clinical and histological examinations are not pathognomonic of lupus erythematosus disseminata, but are rather a manifestation of a severe generalized reaction that accompanies this disease."

W. S. REESE.

Glaucoma

HYDROPTHALMIA. A. GARROW and A. LOEWENSTEIN, Brit. J. Ophth. **25:** 509 (Nov.) 1941.

The authors supply the following summary of their paper:

"A case of hydropthalmia is described clinically and histologically.

"In Bowman's membrane hemispherical bodies, cracks and splits are found.

"Features are described which suggest that Descemet's membrane consists of three layers, a thin layer and two broader layers covering the former. The staining reactions and the appearances at a rupture indicate that the thin anterior layer is the truly elastic part of the membrane and that, developmentally, it may be derived from the posterior corneal lamellae, while the two broader posterior layers are the only part derived from the endothelium.

"The bearing of these observations upon the questions of the regeneration and of the elasticity of the membrane are discussed.

"When the patient was twelve years of age, the eye sustained an accident, which was followed by sympathetic ophthalmitis. The numerous pathological signs of this are mentioned."

A number of illustrations accompany the article.

W. ZENTMAYER.

Lens

CONCERNING THE CHAMBER ANGLE: II. EXFOLIATION OF THE ZONULAR LAMELLA AND GLAUCOMA CAPSULARE. H. S. GRADLE and H. S. SUGAR, Am. J. Ophth. **23:** 982 (Sept.) 1940.

The authors draw the following conclusions from a study of the literature and of 51 cases they have observed:

"From the evidence gathered from the literature, and that presented here, capsular exfoliation is probably a senile degenerative disease, involving the vitreous body and its derivatives, the zonule fibers, and the zonular lamella.

"For some reason, possibly the trauma of the contiguous moving iris, the portion of the anterior capsule in contact with the posterior iris surface develops small vacuoles that tend to separate the lamella into fine laminae. The equatorial zone also shows this process to a lesser degree, possibly due to accommodative stresses. In the area traversed by the pupillary border, the thin laminae are exfoliated as a fine débris that is deposited on the pupillary border, the posterior iris surface, the ciliary processes, the cornea, and the trabeculum. In the last-named location it tends to obstruct the channels for the outflow of the intraocular fluid, and a secondary type of glaucoma—called glaucoma capsulare—

results. In the author's series it was present in 72 per cent of cases. If started early in the course of this condition, the use of miotics to arrest the process may prevent the development of glaucoma. When glaucoma has already developed, antiglaucomatous surgery is indicated. When lens opacities require surgery, the extracapsular operation is recommended. Patients with capsular exfoliation should be made to understand that they may develop glaucoma and should be watched at intervals."

W. S. REESE.

THE MANAGEMENT OF SOME COMPLICATIONS WHICH FOLLOW CATARACT EXTRACTION. E. B. SPAETH, Am. J. Ophth. **23:** 1019 (Sept.) 1940.

Spaeth presents a number of cases of postcataract complications and discusses the management of these complications. The cases include 2 instances of traumatism, 3 of postoperative infection, 3 of subchoroidal hemorrhage, 2 of sympathetic ophthalmia, 5 of iritis (in some of which there was glaucoma) and 4 of different types of prolapse of the iris.

W. S. REESE.

Methods of Examination

THE PROJECTION METHOD OF PRESENTING THE TEST OBJECT FOR TESTING VISUAL ACUITY. C. E. FERREE and G. RAND, Am. J. Ophth. **23:** 882 (Aug.) 1940.

Ferree and Rand give the following summary:

"The projection method of presenting the test object for testing visual acuity affords an easy means of standardizing the intensity of light on the test object and has certain other conveniences for the practicing refractionist. Also it offers a distinct and very great advantage in technique in case of those projectors having special attachments and devices for the detection of errors in refraction, which cannot readily be used with the printed chart. But the unnatural ocular conditions imposed are not good for the testing and rating of vision. Some of these conditions are: a rapidly increasing dark adaptation through the test period, a wider pupil, a sharp brightness contrast of the test field with the dark surroundings (the spotlight object), and a liability to inaccuracies in the focusing of the test object. These points are discussed in the paper. The wider pupil at low illumination in relation to the correction of astigmatism is also discussed."

W. S. REESE.

A STUDY OF PRACTICAL CYCLOPLEGIA. E. J. WENAAS, W. H. EVANS and R. E. ODOM, Am. J. Ophth. **23:** 1123 (Oct.) 1940.

Wenaas, Evans and Odom summarize their studies and present their conclusions as follows:

"Detailed studies in a series of 341 cases show that paredrine hydrobromide [p-hydroxy-α-methylphenethylamine hydrobromide] has no advantage as an adjunct in the production of satisfactory cycloplegia. Neither does paredrine influence the period of accommodative disability following cycloplegia. Paredrine has proved to have some value in producing mydriasis in conjunction with euphthalmine in aged persons.

"These studies have also shown that satisfactory cycloplegia can be produced with minimum quantities of homatropine and atropine, and that smaller quantities have an advantage in shortening the period of accommodative disability. The quantity of cycloplegic used should be individualized according to the patient's age and accommodative function, and not administered by a blanket formula." W. S. REESE.

Neurology

DIAGNOSTIC SIGNIFICANCE OF THE CORNEAL-PTERYGOID REFLEX. A. B. FRENKEL, Vrach. delo **22:** 759, 1940.

Frenkel investigated the corneal-pterygoid reflex in 967 persons, 747 of whom presented disease of the nervous system. Two hundred were normal adults, and 20 were children below the age of 2 years. In persons with a normal nervous system, in neurotic patients and in those with disease of the peripheral nervous system or of the spinal cord the reflex was only seldom present (6 to 7 per cent) and when present was weak. A clearcut corneal-pterygoid reflex was observed only in the presence of a cerebral lesion. It was present with greatest frequency in association with syndromes involving the internal capsule or the motor cortical zone. It appears to be associated with a more or less acute pyramidal lesion. The reflex may be of considerable diagnostic value in cerebral coma, in which it may be active while other reflexes are diminished. It is a reflex of the trigeminal nerve, and its reflex arc is normally inhibited by the pyramidal tracts. It is a manifestation of synergism between the eye and the mouth. The functional relationship is explained on the basis of the philogenetic existence of a single motor apparatus for the eye and the mouth. This apparatus in a later stage of evolution became separated into two distinct functioning apparatuses, that of winking and that of chewing. J. A. M. A. (W. ZENTMAYER).

Operations

TRANSPLANTATION OF CORNEA BY MEANS OF A MECHANICALLY OBTAINED BEVELED-EDGE SEGMENT. M. WIENER and B. Y. ALVIS, Am. J. Ophth. **23:** 877 (Aug.) 1940.

Wiener and Alvis describe their technic of keratoplasty with an ingenious punch which bevels the edges of the corneal graft. This instrument, by means of a bullet-nosed male blade, causes a reversal in the corneal curvature. When cutting is effected by contact with the female blade the edges of the cut cornea are beveled, since a wider cut is made on the anterior than on the posterior surface.

W. S. REESE.

IS A VITAMIN K INSUFFICIENCY CONCERNED IN HEMORRHAGES AFTER INTRAOCULAR OPERATIONS? B. FOSS, Acta ophth. **19:** 15, 1941.

Using a modification of Quick's method for prothrombin determination, the author obtained an average prothrombin time of about twenty-four seconds in a series of 54 patients. Of these, 48 were operated on.

In 12 there occurred either at operation or hours or days later a hemorrhage that could be regarded as greater than normal. None of the patients in whom this occurred showed an abnormal prothrombin time, and the author concludes that K avitaminosis is not a usual cause of bleeding after intraocular operations.

O. P. PERKINS.

Orbit, Eyeball and Accessory Sinuses

RESIDUAL EXOPHTHALMOS AFTER THYROIDECTOMY FOR BASEDOW'S DISEASE. R. A. RAMÍREZ and N. A. HERNÁNDEZ, Arch. de oftal. de Buenos Aires **15:** 58 (Feb.) 1940.

A case is reported of severe residual exophthalmos after thyroidectomy successfully treated by surgical removal of the left upper and middle cervical ganglions and the intervening trunk. A general discussion and a review of the literature follow. The authors consider this treatment preferable to blepharorrhaphy, which is occasionally adopted.

C. E. FINLAY.

Pharmacology

ACTION OF VERITOL SULFATE ON HUMAN EYE: REPORT OF CASES. FRIEMANN, Klin. Monatsbl. f. Augenh. **101:** 563 (Oct.) 1938.

Veritol (2-methylamine-1-parahydroxyphenylpropane) is a preparation resembling epinephrine and chemically related to hordenine and tyramine. Pharmacologic reports on it have been published by Lindner, Rein and Eichler. It has been used to increase blood pressure and to increase blood circulation in connection with surgical measures and medical therapy and in the treatment of tabetic atrophy of the optic nerve by Lauber and Sobanski. Friemann used it in normal eyes and then in glaucomatous eyes for the purpose of testing its effect in the relation of an increase of the blood pressure to lowering of the intraocular tension. He obtained dilatation of the pupil to about 8 mm. thirty minutes after instillation of a 3 or 5 per cent solution. The dilatation lasted for thirty to forty-five minutes. No conjunctival congestion or lesion of the cornea was observed after instillation of a 5 per cent solution; the caliber of the conjunctival vessels remained intact. The intraocular tension was lowered about 3 mm. in healthy eyes. Friemann refers to 4 cases of glaucoma in which the tension was decidedly lowered after other miotics had failed.

K. L. STOLL.

VERITOL FORMIATE, A MYDRIATIC PRODUCING A DECREASE IN INTRAOCULAR TENSION: REPORT OF CASES. R. SCHMIDT, Klin. Monatsbl. f. Augenh. **106:** 429 (April) 1941.

The effect of veritol sulfate on the human eye was reported by Friemann (*Klin. Monatsbl. f. Augenh.* **101:** 563 [Oct.] 1938). The predominant features were mydriasis without cycloplegia and a complete pupillary reaction to light, a decrease in the intraocular tension, dilatation of the palpebral fissure and absence of irritation of the con-

junctiva and of other untoward symptoms. Schmidt reports on a new combination of veritol with formic acid, which he calls veritol formiate [formiate of 2-methylamine-1-parahydroxyphenylpropane]. Essential data from the history of some patients are included in his report, and material on 80 patients is tabulated. Of these, 40 with normal eyes showed dilatation of the pupil up to 7 mm., 28 dilatation of 6 to 7 mm. and 12 dilatation of less than 6 mm. Most of the patients showed mydriasis five to fifteen minutes after instillation of a 5 per cent solution of veritol formiate. This reached a maximum after thirty minutes, lasted one hour and subsided after two to three and one-half hours. Repeated instillations added no further effect or even diminished the effect. The reaction of the pupil to light and on convergence and accommodation remained unaltered. The increase in the palpebral fissure was simultaneous with the mydriasis. No irritation of the conjunctiva or haziness of the cornea was observed, but mydriasis was slight or absent when associated with existing irritation of the conjunctiva. The action of a 5 per cent ointment of veritol was usually less strong but of longer duration than that of an equally concentrated watery solution.

A decrease in the intraocular tension was noted in 5 of 15 persons with healthy eyes. Of 22 patients with glaucoma, the best results with veritol were obtained in those with chronic or secondary glaucoma with slight or no inflammatory changes and no adhesions. The result was less satisfactory in those with secondary glaucoma coupled with iritis and multiple adhesions. No result was recorded for 2 patients with acute glaucoma. Combined treatment with veritol and pilocarpine was effective in some cases in which veritol alone produced no result. In comparison with most other miotics veritol is preferable, because it causes no disturbing miosis.

K. L. Stoll.

Retina and Optic Nerve

Retrograde Degeneration in the Optic Nerves and Tracts. P. J. Leinfelder, Am. J. Ophth. **23:** 796 (July) 1940.

After experiments on cats and monkeys Leinfelder concluded that the visual pathway is not peculiar in its reaction to degeneration but, like other nerves or afferent tracts, reacts to injury by retrograde degeneration in proportion to the extent of injury and to the distance of the injury from the nerve cell. Apparently the disappearance of the nerve fibers in retrograde degeneration occurs after and as a result of the death and disappearance of the ganglion cells.

W. S. Reese.

The Effect of Certain Physical and Chemical Stimuli on the Caliber of the Retinal Blood Vessels in Man. I. Puntenney, Am. J. Ophth. **23:** 1113 (Oct.) 1940.

Puntenney gives the following summary:

"1. Methods for photographing the retinal blood vessels in man have been discussed.

"2. The Kukan ophthalmodynamometer has been used experimentally for lowering the intraocular tension.

"3. New photographic evidence has been presented with the following findings: (a) The inhalation of amyl nitrite in 22 patients produced

dilatation of the veins in two, and a slight dilatation of the arteries in one. (b) Intraocular pressure reduced with the Kukan apparatus in 10 patients produced an increase in the caliber of the veins in eight, with a slight increase in the caliber of the arteries in three. (c) Injections of mecholyl [acetylbetamethylcholine hydrochloride] in eight cases produced a dilatation of the veins in three cases, with a questionable dilatation of the arteries in one. (d) No increase in the caliber of the vessels was observed after nembutal [pentobarbital sodium] and cold pressor tests. (e) One patient photographed during hyperpyrexia treatment showed a questionable dilatation of the veins.

"4. The value of entoptoscopy in determining functional narrowing of the capillaries has been discussed.

"5. The Kukan ophthalmodynamometer has been recommended for massage during treatment following occlusion of the central artery."

W. S. REESE.

A CASE OF GYRATE ATROPHY OF THE CHOROID AND RETINA WITH HYPOGENITALISM. E. C. DAX, Brit. J. Ophth. **25:** 18 (Jan.) 1941.

The patient, a man, was 72 when the condition was first noted. The left eye was blind from the sequelae of a trauma. The right eye was blind and showed gyrate atrophy of the choroid and retina of the multiple colobomatous type. The interesting features were an absence of myopia, the fact that the condition was first apparently noticed late in life, the presence of associated hypogenitalism and obesity and failure of the urine to disperse the melanosomes of the frog.

The article is illustrated.

W. ZENTMAYER.

A CASE OF JUVENILE AMAUROTIC IDIOCY WITH DISTURBANCES IN WATER-SALT METABOLISM. E. C. DAX, Brit. J. Ophth. **25:** 24 (Jan.) 1941.

Dax reports a case of juvenile amaurotic idiocy in a girl whose sister was similarly affected. There were mild arachnodactyly and other abnormalities associated with this condition; in particular there were differences in the size and color of the nipples and areolas, abnormal heart sounds, laxity of ligaments, kyphosis and abnormal length of the arms and legs as compared with the trunk. Five cousins had long digits. An abnormality of the water-salt metabolism was shown by a retention of sodium chloride on test and a delay in urinary secretion in response to a urine dilution test.

The article is illustrated.

W. ZENTMAYER.

EXPERIMENTAL PIGMENTARY DEGENERATION OF THE RETINA BY SODIUM IODATE. A. SORSBY, Brit. J. Ophth. **25:** 58 (Feb.) 1941.

Sorsby gives an account of pigmentary degeneration of the rabbit's retina induced by intravenous injection of 5 cc. of 2 per cent solution of sodium iodate. He reported that the essential lesion was damage

to the neuroepithelium, the pigmentary changes being absent in the albino rabbit, and that, furthermore, in doses sufficient to induce retinal damage sodium iodate acted as a selective poison of the retina.

The author provides the following summary of his article:

"1. A review is given of the clinical cases in which the use of septojod [a German iodine preparation containing sodium hypoiodite and sodium hypoiodate] led to transient or permanent loss of vision from pigmentary changes in the retina.

"2. The experimental work leading to the incrimination of sodium iodate as the toxic agent is indicated.

"3. The dosage for the experimental production of pigmentary degeneration of the retina in the rabbit is shown as 5 cc. of the 2 per cent solution injected intravenously.

"4. There is no evidence that with this dosage there is any permanent damage to other tissues, so that sodium iodate may be regarded as a selective poison to the retina.

"5. By means of the method of vital staining with Kiton Fast Green it is shown that the retina is damaged by iodate in the albino rabbit though no pigmentary disturbances are seen ophthalmoscopically."

The article is illustrated.

W. ZENTMAYER.

THE NATURE OF EXPERIMENTAL DEGENERATION OF THE RETINA. A. SORSBY, Brit. J. Ophth. **25:** 62 (Feb.) 1941.

Sorsby refers to the preceding paper (*Brit. J. Ophth.* **25:** 58 [Feb.] 1941) and questions whether the results presented do not indicate that some specific retinal metabolic process was disturbed by the sodium iodate. From experimental data the suggestion emerges that iodate probably acts by virtue of its oxidizing properties and that the different appearances of the lesions produced by another oxidizing agent, sodium perborate, were probably due to the different rate of action, to the amount of perborate in the doses and to the methods taking longer to induce visible changes.

Sorsby concludes as follows:

"What significance these findings have in the interpretation of the range of pigmentary changes seen clinically, is difficult to assess. That two different oxidizing agents should produce changes simulating retinitis pigmentosa in one case and chorio-retinitis in the other, raises the question as to whether clinically observed pigmentary changes with their great ophthalmoscopic variations, are not fundamentally identical lesions, modified by a different rate of development. There is no inherent improbability in the suggestion that retinitis pigmentosa is caused by an inborn metabolic disorder and chorio-retinitis by comparable tissue-poisons introduced extraneously. . . . The results described have not been checked and they are published as a preliminary and unverified note."

The article is illustrated.

W. ZENTMAYER.

IMPORTANCE OF ELEVATION OF THE RETINA IN LOCALIZATION OF RETINAL TEARS. E. LOBECK, Arch. f. Ophth. **142:** 82, 1940.

Retinal tears are localized by determining their longitude (the meridian) and latitude (their distance in an anteroposterior direction from any of the landmarks of the eye, usually the limbus). The estimation of the longitude either by Gonin's or by Weve's method has proved accurate and reliable, whereas the latitude as determined by either of these two methods often proves incorrect. The chief source of error is the elevation of the retina, which by a number of authors has not been taken into consideration. From simple diagrammatic drawings it can be learned that the choroidal area which corresponds to a retinal tear or against which the tear will come to lie after evacuation of the subretinal fluid lies anteriorly (toward the limbus) to the choroidal area which during ophthalmoscopic examination of the elevated retina appears to lie in line with the tear. The correct latitude of a tear situated in a markedly elevated retina, whether it is determined after Gonin's method by estimating its distance in disk diameters from the limits of the ophthalmoscopic field, by measuring perimetrically the angle between the visual axis and the observer's line of sight to the lesion or during operation by the transillumination method of Weve, can be found only if allowance is made for the elevation of the retina. By a simple mathematical method Lobeck has worked out correction factors which have to be subtracted from the apparent distance between ora serrata and tear in order to obtain the correct latitude of the tear.

Practically, the procedure is as follows: The apparent distance from the ora serrata to the tear is estimated in disk diameters. The elevation of the retina is measured by determining the refraction of the tear and that of the choroid visible through the tear by direct ophthalmoscopy. In Lobeck's tables (one for the emmetropic, one for the moderately myopic and one for the highly myopic eye) the proper corrections can be found for varying retinal elevations and for distances from ora serrata to tear.

In a similar way G. H. Stine, in a paper (Tables for Accurate Retinal Localization, *Am. J. Ophth.* **17:** 314, 1934) not quoted by Lobeck, approached the problem of the elevation of the retina as a factor in the localization of retinal tears. P. C. KRONFELD.

Tumors

METASTATIC MALIGNANT MELANOMA OF THE RETINA. E. M. UHLER, Am. J. Ophth. **23:** 158 (Feb.) 1940.

Uhler reviews the literature and reports a case of metastatic involvement of the retina by a malignant melanoma without involvement of the optic disk or the choroid. W. S. REESE.

METASTATIC CARCINOMA OF THE IRIS. M. K. ASBURY and D. VAIL, Am. J. Ophth. **23:** 402 (April) 1940.

A 49 year old white woman, married, had had her right breast and axillary lymph nodes resected because of a malignant process. Shortly

afterward a tumor appeared in the right iris and began slowly to increase in size. A spongy yellow-white new growth almost filled the temporal third of the anterior chamber. The floor of the anterior chamber was filled with yellow-white gelatinous and globular debris, and the tension was 65 (Schiötz). Enucleation was done and the diagnosis of metastatic carcinoma of the iris verified. W. S. REESE.

PROGNOSIS IN SARCOMA OF THE UVEA. T. R. PAHWA, Brit. J. Ophth. **25:** 241 (June) 1941.

For the purpose of investigation, the author chose 100 patients with sarcoma of the uvea admitted to the Royal London Ophthalmic Hospital (Moorfields) during the years 1930 to 1935 inclusive. This period was chosen, first, because considerable difficulty is experienced in tracing hospital patients after the lapse of a long period and this period is not too long (although even after it a certain number of patients could not be traced). Second, the majority of patients in this series had been operated on more than five years before and none less than three years before; so sufficient time had elapsed to make possible the conclusion that the majority who had escaped metastasis thus far had in all probability escaped it permanently. Third, 100 patients is a number large enough to make the results of some value.

The choroid was involved in 83 patients, the choroid and ciliary body in 13 and the iris in 4.

The author draws the following conclusions:

"From the preceding pages and the facts and figures quoted therein it seems reasonable to infer that Callander [Callander, G. R.: Malignant Melanotic Tumours: Histological Study of Types in 111 Cases, *Tr. Am. Acad. Ophth.* **36:** 131-142, 1931] and Callander and Wilder [Callander, G. R., and Wilder, H. C.: Melanoma: Prognostic Significance of Argyrophile Fibres, *Am. J. Cancer* **25:** 251 (Oct.) 1935] have made a very important contribution towards the solution of this very vague problem, the prognosis in sarcoma of the uvea. It also seems reasonable to conclude from the authors quoted in the previous chapter, that good results in many cases are due, not so much to early diagnosis and treatment, as to other factors, such as reticulin content of the growth and its histological type. Early diagnosis does play a part, but a subsidiary part only, as there are many cases in which the diagnosis and enucleation were carried out in the first stage of the disease, yet the patient succumbed to secondary growths. From the series published by Callander, Terry and Johns [Terry, T. L., and Johns, J. P.: Uveal Sarcoma—Malignant Melanoma, *Am. J. Ophth.* **18:** 703 (Oct.) 1935] and McKee [McKee, S. H.: Primary Sarcoma of the Uveal Tract, *Canad. M. A. J.* **36:** 361 (April) 1937] histological cell-type classification has definitely established a place for itself in the pathology of the uveal sarcoma, I mean as regards the prognosis, the same, however, cannot yet be said of the reticulin content basis. For the latter further records and statistics over a large number of years are necessary.

"To recapitulate, three grades of malignancy can be distinguished from the histological types:

"Grade I.—Spindle type A, comparatively a benign type, in so far as if other circumstances such as early diagnosis and treatment are

favorable, there is hardly any death recorded from metastases in this group.

"Grade II.—Spindle type B, more malignant than type A, but less malignant than other types.

"Grade III.—Fascicular, epithelioid, and mixed-cell types, very much more malignant than the other types, showing a mortality of about 40 per cent, the last named is more malignant than the other two.

"Reticulin content seems to influence the prognosis considerably, and it is possible by the examination of argyrophile fibres to determine the prognosis very much more accurately, as to which patient is likely to survive from, and which patient is likely to succumb to, metastases in malignant types.

"From the examination of both, that is combined study of histological types and reticulin, it should be possible to foretell the prognosis in a very large number of cases, further checking and rechecking is required before a final verdict is delivered. As I have quoted several times in the text following these cases for a period of 3 to 8 years is not sufficient, as many observers have shown that metastases occur after this period.

"The total mortality from secondary growths in this series works out at approximately 30 per cent, E. von Hippel records that it is 45 per cent., he has of course followed his cases over a large number of years, some of them for over 20."

The article is illustrated.

W. ZENTMAYER.

PROGNOSIS IN RETINAL GLIOMA AND UVEAL SARCOMA. R. TÜSHAUS, Klin. Monatsbl. f. Augenh. **105:** 41 (July) 1940.

The author investigated the fate of 30 patients with glioma or uveal sarcoma whose eyes were examined histologically at the Pathologic Institute of Düsseldorf. Of the glioma of 10 patients, that of 7 was discovered between the ages of 1 and 3 years, that of 2 between 4 and 6 years and that of 1 at 34. Bilateral glioma was found in 1 patient. Data in a table show that 9 of 10 patients remained free from recurrences or metastases during an observation period varying in length to nine years. In the author's opinion this favorable record was due to early enucleation. Roentgen irradiation as the only therapy was not satisfactory, and radium therapy proved a complete failure.

A table furnishes data on 19 patients with intraocular sarcoma and 1 with neurofibroma. Some of these patients were observed as long as ten years. One was 4 years old, and 2 were in the third decade of life, 3 in the fourth, 8 in the fifth, 4 in the sixth and 1 in the seventh. The fact that most of the patients were in the fifth and sixth decades conforms with the observations of other authors. Local recurrences appeared to be rare, but metastases were observed after early enucleation of very small tumors. Irradiation and radium therapy failed. Early and radical operation is indicated for both types of tumor discussed.

K. L. STOLL.

MELANOSIS OCULI, WITH MELANOSARCOMA. O. CARLBERG, Acta ophth. **18:** 301, 1940.

A man of 45 with clearcut signs of melanosis of the left eye had a richly pigmented sarcoma of the choroid. Diagnosis of the growth was

made clinically by its appearance and its failure to become transilluminated and was confirmed by histologic examination. The melanosis, also confirmed microscopically, had been present throughout the patient's life.

O. P. PERKINS.

Uvea

PIGMENTED CHOROIDAL VESSELS (SIEGRIST). U. THORDARSON, Acta ophth. **18:** 383, 1940.

The author has observed 7 cases of pigmented choroidal vessels, a rare lesion of the fundus of which only 15 other cases have been recorded.

All the cases have been strikingly similar to those originally observed by Siegrist in 1889. The patients averaged 60 years in age and for the most part showed signs of generalized vascular disease, hypertension and renal involvement.

The typical lesion consists of beadlike accumulations of black pigment arranged in linear streaks and radiating toward the periphery from a region around the optic disk. The streaks never extend beyond the equator, and each seems to follow the course of an underlying choroidal vessel. The pigment is thought to be derived from the pigment epithelium, and the author believes it likely that the formation of streaks is secondary to the effects of hypertension, but he cannot explain the characteristic form.

There are several photographs and a drawing depicting this strange lesion of the fundus.

O. P. PERKINS.

Visual Tracts and Fields

HOMONYMOUS HEMIANOPIA. E. ADROGUÉ, Arch. de oftal. de Buenos Aires **14:** 584 (July) 1939.

The author presents his experience in a large number of cases of hemianopia in which the visual fields were measured by quantitative perimetry and in all except 10 of which the diagnosis was confirmed anatomically or surgically.

He first considers in detail the course of fibers in the optic tracts. He holds that they all pass to the external geniculate body and believes the statement that the pupillary fibers do not enter the external geniculate body to be in error. He describes the segmentary arrangement of the external geniculate body, with the relations of the segments, and the optic radiation, with its relations to other intracerebral tracts and structures. His description differs entirely from that of Gratiolet. The efferent fibers of the fifth dorsal and fifth ventral layers constitute the *radiatio cellularum gigantium* (Balado), which leaves the optic radiation and forms the major part of the *brachium quadrigeminum superium,* entering the anterior quadrigeminal tubercle. This he considers the pathway of the pupillary reflex.

He next takes up the development of the occipital lobe. In primates the area striata is limited to the calcarine fissure and the apex of the occipital lobe, there being variations according to species and individuals. As to the retinal projection on the area striata, present knowledge

is not precise. It is known that the upper half of the retina is projected on the superior, or cuneal, lip, and the lower half on the inferior, or lingual, lip, the peripheral portion of the visual field being located in the frontal, or anterior, portion. The author describes a case of his own in which homonymous peripheral scotomas just below the horizontal meridian were produced by a lesion of the superior lip of the calcarine fissure incurred during a ventricular puncture. He does not accept Henschen's theory of retinal projection, considering that the macula occupies a determined portion of the area striata. He discusses the different opinions related to the so-called sparing of the macula; he believes that if an examination is made with the proper precautions in the case of a lesion of any part of the visual pathways no such sparing of the macula is revealed and that the apparent sparing (of 1 to 2 degrees in a $\frac{1}{2.000}$ isopter) is to be found with both pregeniculate and postgeniculate lesions. As to the defect in the temporal part of the monocular visual field, of which the author's case continues the sole anatomic confirmation, there are clinical observations by other authors, mostly reported in cases of cortical excitation in scintillating scotoma.

With regard to the classification of hemianopic visual field defects, while recognizing the value of Wilbrand's thirty types, the author thinks that any lesion affecting the visual pathway posterior to the chiasm will produce a hemianopic visual field defect, the differential localization depending on the condition of the ocular fundus, the pupillary reflexes, the form of the defect and the accompanying symptoms. As to symptoms, he considers the hemianopia of vascular origin, with the symptoms related to the visual field defect and the lesions produced by a cerebral tumor.

The types of hemianopia classified according to the site of the lesion include cortical blindness with double hemianopia, conjugate deviation with hemianopia and scintillating scotoma with migraine and hemianopic hallucinations.

This extensive paper is illustrated with numerous visual field charts and clinical observations and is accompanied by an extensive bibliography. Justice to it in an abstract is scarcely possible.

C. E. FINLAY.

Society Transactions

Edited by Dr. W. L. Benedict

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Secretary*

October 16, 1941

Molluscum Contagiosum with Corneal Complications: Report of Two Cases. DR. T. H. COWAN.

A brief résumé was presented of the general and ophthalmologic aspects of molluscum contagiosum, together with a digest of the literature pertaining to complications which occur in the eye as a result of this disease. Two cases were reported in which molluscum contagiosum of the border of the lid was associated with chronic conjunctivitis and multiple superficial erosions of the cornea.

DISCUSSION

DR. W. BRAUN, Merchantville, N. J. (by invitation): It is a privilege to have listened to Dr. Cowan's excellent presentation, and it might be of interest to report a similar case I had the opportunity of observing at the Cooper Hospital clinic, Camden, N. J., a few years ago. The patient was a small child. The mother stated that she had noticed white fleshlike growths on the right upper lid for about a month. The lesions were suggestive of molluscum contagiosum. Dr. J. S. Shipman was called in consultation, and he suspected this disease. He suggested that the patient be seen by Dr. Zentmayer, who confirmed the diagnosis.

Examination revealed several small fleshlike semiglobular masses on the right upper lid, one of which was near the margin. All had the typical umbilicated center. Mild blepharitis and a chronic type of conjunctivitis were also present. Dr. Zentmayer suggested curetting the lesions and cauterizing their bases with tincture of iodine. This was done, and the condition cleared up remarkably well. The conjunctivitis subsided within a few days.

I was interested to learn of the associated corneal lesions in the cases Dr. Cowan reported. As far as I know there were no corneal lesions in the case I have mentioned, although microscopic examination with the slit lamp was not done.

DR. T. H. COWAN: I wish to thank the commentator for his remarks, and in closing I should like to add that a diagnosis of molluscum contagiosum can be made readily by the pathologic appearance of the lesions, which resemble those of no other cutaneous condition.

Grossly, molluscum contagiosum must be differentiated from the common wart, probably from the sole sebaceous cyst and also from an enlarged pore containing a plug of sebaceous material.

Ocular Findings in Patients with Diabetes Mellitus in Whom the Disease Was Controlled for Ten Years. DR. I. H. LEOPOLD.

A report was made concerning the examinations of 100 persons with diabetes who had been closely observed and treated for over ten years. These patients had been under the care of Dr. Russell Richardson at the metabolic clinic of the Hospital of the University of Pennsylvania. All had been kept on a diet high in carbohydrates and low in fats. Sufficient insulin had been administered to maintain a satisfactory blood sugar level.

At the end of the ten year period the eyes were examined chiefly with respect to visual acuity, pupillary reaction and tension and for corneal wrinkles and pigmentation, iritis and iritic depigmentation, retinal hemorrhages and exudates, sclerosis and optic atrophy and neuritis.

The results were compared with those published previously with statistics evaluating therapy. The conclusions drawn were as follows: The folds in Descemet's membrane were reduced by adequate therapy, but motility of the ocular pigment was unaffected by therapy. The incidence of iritis, muscular palsy, optic neuritis and atrophy and abnormal pupillary reactions was uninfluenced by therapy. Lenticular changes of the senile type had the same incidence as in a group of nondiabetic persons of the same ages. Subcapsular flocculi persisted in spite of therapy. The incidence of complicated cataract was reduced. The incidence of retinal sclerosis was the same as that for nondiabetic persons. Deep punctate hemorrhages and waxy exudates increased in incidence as the duration of the diabetes increased and were slightly reduced by therapy. A reduction in visual acuity and an increase in superficial hemorrhages can be expected with an increase in the duration of the diabetes in spite of therapy.

Although arteriosclerosis, hypertension, sepsis, hyperglycemia and renal damage all influence deep retinal hemorrhages, not one is the sole etiologic factor.

DISCUSSION

DR. WILLIAM ZENTMAYER: It might be of interest to know whether there were any patients with hemianopia in the group reported on. Some years ago Dr. de Schweinitz presented before this section a paper concerning hemianopia associated with diabetes.

DR. WARREN S. REESE: Did Dr. Leopold notice any relationship between retinal disease and lenticular capacity?

DR. WILLIAM ZENTMAYER: Was he able to confirm the presence of aneurysmal dilatations in the veins in cases of diabetic retinitis, as reported by O'Brien and Allen?

DR. W. I. LILLIE: I wish to congratulate Dr. Leopold on his excellent report on a well studied group of diabetic patients. My curiosity is similar to that of Dr. Zentmayer; that is, in the light of recent studies concerning venous sclerosis as an early manifestation of diabetes, was this observed in any of Dr. Leopold's cases?

Flame-shaped hemorrhages and cotton wool exudates are best explained on the basis of associated arteriolar hypertension and are not characteristic of diabetes. The punctate hemorrhages and exudates are the result of thrombosis of the capillaries and venules, which are situated deeper than the retinal vascular layer.

In what percentage of the cases were venous changes observed?

DR. ALFRED COWAN: I am particularly interested in changes in the iris. I am not sure whether I missed a discussion of these in the report or whether the ages of the patients in whom changes had occurred in the posterior surface of the cornea and in the pigment of the iris were not given. I am interested in knowing whether such changes occur more often in young diabetic patients than in nondiabetic patients and whether they occur more often in treated than in untreated diabetic persons. The changes in pigment, absorption and so forth represent a normal senile process. However, it is usually considered that changes in pigment in the iris are more likely to occur in persons with diabetes.

I should like to know whether the changes in the iris and in the posterior surface of the cornea are in the pigment. They occur frequently in young diabetic persons and are seen in ordinary senility.

Occasionally a diagnosis will be made immediately when the aqueous becomes inky with pigment after the anterior chamber has been opened.

DR. FRANCIS HEED ADLER: Such an interesting study is of value only if care is taken in interpreting the statistical findings. Since there are so many variables which cannot be controlled, considerable caution must be exercised in drawing conclusions, and I feel that Dr. Leopold has shown such caution.

The outlook for the diabetic patient seems rather discouraging according to this study. The clinician is now in a position to prolong his life by such measures as were used in the cases reported, but treatment apparently has little influence on the retinal changes. The essential factor in the development of these seems to be the duration of the disease; whether the disease is controlled or not makes little difference.

If clinicians are successful in prolonging the lives of diabetic patients more patients will be visually incapacitated unless the cause of diabetic retinopathy is discovered.

DR. I. H. LEOPOLD: The visual fields were examined only in cases in which there was some indication of optic atrophy or neuritis or retrobulbar neuritis. These numbered 24. Among them were no cases of scotoma or hemianopia. Aneurysmal dilatations were looked for, but none were found. Rubeosis diabetica was also looked for but not observed.

The question concerning the fulness and the sclerosis of the retinal veins as possible etiologic factors in deep punctate hemorrhages can be answered as follows: Observation of venous changes was attempted, and it was difficult to evaluate the size of the retinal veins, especially of the third division of these veins. This division was discussed by I. C. Michaelson and A. C. P. Campbell (Anatomy of the Finer Retinal Vessels, *Tr. Ophth. Soc. U. Kingdom* **60:** 71, 1940). Because of the difficulty encountered in evaluating venous changes, no reliable statistics can be given with respect to them for this group of diabetic patients.

Depigmentation was seen mostly in the older patients, as in those reported by Waite and Beethan.

In answer to Dr. Reese's question, I must admit that we have not yet analyzed the statistics with regard to relationships between lenticular changes and retinal change.

The Superior and Inferior Oblique Muscles. DR. W. E. KREWSON.

The oblique muscles present many interesting contrasts. The superior oblique muscle arises at the optic foramen and is the longest muscle in the orbit; the inferior oblique muscle arises at the inferior orbital foramen and is the shortest. The former has the longest tendon of all the external ocular muscles but no check ligament, while the latter has no tendon but has the longest check ligament. The superior oblique muscle has the most variable insertion, usually on the vertical meridian, anterior to the vortex veins; the inferior has the most constant insertion, located on the horizontal meridian and posterior to the vortex veins.

The arc of contact for the superior oblique muscle is shorter than that for any of the other muscles; that for the inferior, the longest. The superior oblique muscle has a contralateral innervation and the inferior an ipsilateral or bilateral representation. The superior acts as a depressing muscle and the inferior as an elevator. Their respective actions increase as the eye is turned inward and decrease as the eye is turned outward. The former acts as an intorter and the latter as an extorter. Both torsional actions increase as the eye is turned outward and decrease as it is turned inward.

Both muscles are reputed to act as external rotators, their action increasing as the eye is turned outward and decreasing as the eye is turned inward. There still may be a question, however, as to whether the inferior acts as an internal or as an external rotator. The superior is the second most frequently paralyzed muscle; the inferior is the least often involved, but when it is involved the paralysis is often accompanied by internal ophthalmoplegia.

Limitation of movement and vertical diplopia are greatest in paralysis of the superior oblique muscle when the eye is turned down and in and in paralysis of the inferior oblique muscle when the eye is turned up and in. Vertical diplopia is greater in paralysis of the inferior than in that of the superior oblique muscle. In paralysis of the superior oblique muscle the false image is inclined toward the normal side, while in paralysis of the inferior oblique muscle the false image is inclined toward the affected side.

Misdirection of Regenerating Third Nerve Fibers: Surgical Correction. DR. E. B. SPAETH.

Moving pictures were shown which represented various oculomotor defects resulting from misdirection of regenerating fibers of the third nerve. The outstanding point of interest was that the fibers normally destined for the inferior rectus muscle terminated in the sphincter iridis. The fibers for the sphincter iridis normally enter by way of the short root to the ciliary ganglion from the nerve supply to the inferior oblique muscle. The misdirection could have been twofold; that is, the fibers

for the inferior oblique muscle passed into the inferior rectus muscle and fibers for the the inferior rectus muscle passed into the ciliary ganglion.

Examination of patients with paretic mydriasis revealed definite contraction in downward rotation; at the same time the levator muscle contracted, lifting the lid. This action was also present with the contraction of the internal rectus muscle, but to a much less degree. Otherwise the lid was held in repose or in ptosis.

Operation on the paretic internal rectus muscle and recession of the external rectus muscle were performed simultaneously. The levator muscle was completely detached from the tarsal plate. Several weeks later the ptosis was corrected by transplanting orbicularis muscle to the occipitofrontalis muscle. After the operation the diplopia was absent except during extreme elevation and depression.

For diplopia which continues as a disabling factor it is planned to limit the arcs of contact for the vertically functioning muscles in the good right eye, thereby limiting their excursions.

These surgical procedures carried out apply equally well to the ptosis which is seen in the jaw-swinging reflex.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Brazilian Ophthalmologists Form Examining Board.—The Brazilian Board of Ophthalmology was recently established and began to function January 1. Dr. Cesario de Andrade, Rio de Janeiro, is president, and Dr. Moacyr E. Alvaro, São Paulo, is secretary. The board is made up of professors and assistant professors of ophthalmology from all the Brazilian universities, the presidents of all Brazilian societies of ophthalmology and a representative of the Pan-American Congress of Ophthalmology.

The board will certify the older recognized ophthalmologists without examination, as did the American Board of Ophthalmology in its infancy. The second group to be certified without examination will be the younger ophthalmologists who have been in practice for a minimum of two years and who submit a monograph especially prepared for the occasion on some subject pertaining to ophthalmology. All other ophthalmologists will be required to pass an examination similar to that of the American Board of Ophthalmology. The fee for the examination will be $50.

The Brazilian Board of Ophthalmology has requested that the Brazilian government issue a decree that henceforth all ophthalmologists holding governmental positions possess the certificate of the board. It is probable that this request will be granted.

At the meeting of the American Academy of Ophthalmology and Otolaryngology in October 1941 the council voted that any Brazilian holding a certificate of the Brazilian Board of Ophthalmology will be eligible to membership in the academy.

Brazilian Quarterly Becomes Official Journal for Ophthalmologic Congress.—*Ophthalmologica Ibero-Americana,* the Brazilian quarterly abstract journal, is now the official organ of the Pan-American Congress of Ophthalmology. *Ophthalmologica* has appeared only in Portuguese, but after January 1 all abstracts will be printed in Spanish and English or in Portuguese and English. Original articles, reports of scientific activities of the congress, news items and so on will be reproduced in all three languages. Dr. Moacyr E. Alvaro, São Paulo, Brazil, is managing editor, and the committee on literary exchange of the congress, consisting of all the ophthalmologic editors of the Western Hemisphere under the chairmanship of Dr. J. Lyo Pavia, Buenos Aires, Argentina, forms the editorial board. *Ophthalmologica Ibero-Americana* will be sent without charge to all members of the Pan-American Congress of Ophthalmology who have paid dues in advance. An annual membership fee of $5 will be sufficient to supply the journal to all members and to finance the second Pan-American Congress of Ophthalmology, which is to be held in Montevideo, Uruguay, in November 1943. Interested ophthalmologists are asked to send their names and addresses together with the

membership fee of $5 to Dr. Conrad Berens, secretary-treasurer of the Pan-American Congress of Ophthalmology, 411 First Avenue, New York.

The de Schweinitz Memorial Fund.—The friends and former associates of George E. de Schweinitz plan to equip and furnish a room in the Hospital of the University of Pennsylvania, Philadelphia, to serve as a Library of Ophthalmology and to be known as the de Schweinitz Memorial Library. It will contain Dr. de Schweinitz' collection of medical books which he gave to the University of Pennsylvania School of Medicine, and when completed it will be open to physicians and medical students and will comprise one of the best collections of ophthalmologic literature in this country.

The cost of remodeling the room is estimated at $5,000. It is hoped that all of Dr. de Schweinitz's friends will contribute toward the realization of this goal, and any donation toward the sum, large or small, will be gratefully accepted so that a memorial worthy of him will be created.

Checks should be made payable to "Trustees of the University of Pennsylvania" and sent to the de Schweinitz Fund, 3446 Walnut Street, Philadelphia.

Postgraduate Week, New York Eye and Ear Infirmary.—The Postgraduate Week of the School of Ophthalmology and Otolaryngology of the New York Eye and Ear Infirmary will be held March 23 to 28 inclusive. There will be clinical and practical demonstrations and lectures in various phases of ophthalmology and otolaryngology. Guest speakers for ophthalmology will be: Drs. Derrick Vail, Cincinnati; Edmund B. Spaeth, Philadelphia; Albert D. Ruedemann, Cleveland; Algernon Reese, New York, and members of the staff of the New York Eye and Ear Infirmary.

Clinical Congress of the American College of Surgeons.—Because of the war, the thirty-second annual Clinical Congress of the American College of Surgeons will be held in Chicago, October 19 to 23, instead of in Los Angeles, as originally planned. Headquarters will be at the Stevens Hotel. The twenty-fifth annual Hospital Standardization Conference sponsored by the College of Surgeons will be held simultaneously. The programs of both meetings will be based chiefly on wartime activities as they affect surgeons and hospital personnel in military and civilian service.

Research Study Club of Los Angeles.—At the eleventh annual midwinter postgraduate clinical course in ophthalmology of the Research Study Club of Los Angeles, held January 19 to 30, Dr. Ralph I. Lloyd, of Brooklyn, was the main guest speaker for ophthalmology. Dr. Lloyd, the present president of the American Academy of Ophthalmology and Otolaryngology, not only is a recognized pioneer in modern ophthalmology but is a superb teacher, with many subjects at his command.

SOCIETY NEWS

New York Society for Clinical Ophthalmology.—At the meeting to be held March 2 there will be a panel discussion on "Disturbances of Ocular Motility" by Drs. George P. Guibor, LeGrand H. Hardy,

Luther C. Peter and James W. White. The coordinator will be Dr. Isador Givner. The panel discussion will be preceded by a paper on "Neuro-Ophthalmological Aspects of Eye Muscle Disorders" by Dr. Israel S. Wechsler.

The meeting will be held at the Squibb Hall, 745 Fifth Avenue, New York city, and all ophthalmologists are cordially invited to attend.

Reading Eye, Ear, Nose and Throat Society.—At the meeting held Dec. 17, 1941, at Reading, Pa., the following films in color and sound were shown by Dr. Samuel J. Kopetzky: "Otoscopy in the Inflammations" and "A Clinic on Petrositis."

At the meeting of the society held on January 21, Dr. Ramon Castroviejo presented the following films: "Dacryocystorhinostomy," "Cataract Extraction by Suction," "Ptosis Operation by the Use of the Levator," "Keratoplasty" and "Tattooing of the Cornea with Gold Chloride."

CORRECTION

In the article by Drs. Thomas D. Allen and Walter G. Ackerman entitled "Hereditary Glaucoma in a Pedigree of Three Generations," in the January issue (ARCH. OPHTH. **27:** 139, 1942), several errors occurred.

On page 147, in the third line from the last "eighteen" should read "twelve" and in the next to the last line "first" should read "second."

On page 149, in the paragraph headed "Second Generation," near the end of the fifth line, after "excavations of" "7 diopters of" should be inserted; in the sixth line, "— 1" should read "+ 1"; in the seventh line, "May 24" should read "April 6" and "Feb. 3, 1907" should read "May 24, 1906." At the end of the eighth line should be inserted "There is no record of iridectomy on the left eye."

On page 155, in the third line from the bottom, "22/20" should read "20/20"; in the tabulation, 6/10/39 and 6/13/39 should be 7/10/39 and 7/13/39, and 7/13/40 should be 7/15/40.

The legends for some of the visual fields and tonometric charts have been transposed. If the illustrations are left in their present positions and with their present numbering, the correct legends for charts 3 to 9 are:

[On page 151]

Chart 3.—The visual fields of Ione S. (third generation).

[On page 152]

Chart 4.—The visual fields of Jean S. (third generation).

Chart 5.—The visual fields of David S. Jr. (third generation).

[On page 153]

Chart 6.—The tonometric chart of Miriam S. (third generation).

In the tonometric charts the unbroken line indicates the right eye and the broken line the left eye.

Chart 7.—The tonometric chart of Ione S. (third generation).

[On page 154]

Chart 8.—The tonometric chart of Jean S. (third generation).

Chart 9.—The tonometric chart of David S. Jr. (third generation).

These and some minor changes will appear in the authors' reprint, a copy of which may be procured from them.

Book Reviews

Reading Readiness. By M. Lucille Harrison, Colorado State College of Education. Pp. 166. New York: Houghton Mifflin Company.

This book of five chapters, an appendix and an index is a discussion of the factors influencing reading readiness, how to foster them, test for them and handle children who lack them. It combats vigorously the assumption that if a child does not read at the time reading is introduced, he is either stupid or lazy or perhaps cannot see or hear.

The essential values of the book are contained within the first hundred pages, wherein are discussed the factors influencing reading readiness, instruction fostering reading readiness and a testing program for reading readiness. Each chapter contains a terminal summary of the discussion. Following a short introduction, the second chapter, dealing with factors influencing reading readiness, largely combats the prevalent idea that all children are ready for reading at the chronologic age of 6 years. The author maintains that the child should not progress from kindergarten to the first grade until the probability of success in reading is assured. Development, mental, physical and personal, to an adequate level is a prerequisite for a successful reading program. The author lays particular stress on six factors: (1) adequate mental age, (2) good vision, (3) good hearing, (4) emotional stability, (5) adjustment to the school situation and (6) the seven abilities which should result from the preparatory period of instruction in reading. These abilities and methods for their cultivation form the subject matter of the third, and extremely practical, chapter of the book. It is a description of the modern school (kindergarten and first grade) technic.

Chapter 4 outlines a testing program for reading readiness. Eight mental maturity tests are mentioned but not described. Five tests of readiness for reading are discussed and evaluated. They are the Betts tests, the Lee Clark tests, the Metropolitan tests, the Monroe aptitude tests and the Van Wagenen tests. The evaluation of these various tests is excellent, and one would probably not go far astray in regarding the tests ascendingly in the order given, with the Van Wagenen tests properly and carefully carried out yielding the most valid results, although the author makes no such commitment.

The final chapter discusses placement and the remedial program. It is largely tabular, listing signs and symptoms relating to various factors and suggesting therapeutic measures.

I believe the author has performed a commendable piece of work in producing this introduction to, and handbook of, reading readiness. Certainly for the ophthalmologist, who is here primarily concerned, it is a clearcut presentation of an unfamiliar field, and not the least to recommend it is its freedom from pessimism. LeGrand H. Hardy.

The Retina. By S. L. Polyak, M. D. Price, $10. Pp. 607. Chicago: University of Chicago Press.

Dr. Polyak has gathered together in one volume the results not only of his own researches but of those of the host of investigators of the finer structural elements of the retina. An extensive, thorough-going treatise on the primate retina, it is saved from unwieldiness by the excellence of its arrangement.

The some 600 pages are divided into six parts, the largest and most important dealing with the minute structure of the retina, the cytologic structure of the various elements and their distribution in the foveal and peripheral regions. The author writes at length on the synaptic relations between the rods and cones and the bipolar cells, of which he describes several distinct types. Similarly, the neural relationships of associational, amacrine and ganglion cells are discussed in detail. In the discussion of this subject and the conflicting concepts of it, a service is rendered alike to the investigator, the teacher and the student.

There is an excellent dissertation on the peculiar requirements of the retina as to histologic technic. The methods, their limitations and their advantages are discussed and detailed instructions given for their application; this discussion will be especially appreciated in the laboratory.

The history of the development of knowledge of the retina is of unusual interest and is accompanied by a number of reproductions of early and little known diagrams of the eye. Considerable emphasis is given the Arabian contributions.

The one hundred plates at the end of the text, mostly of the author's preparations, while ample and clear, might have been more helpful with the addition of some text figures.

Such a volume might seem mainly of value to the specialist in a somewhat narrow field, but the histologist, the neuroanatomist and the clinical ophthalmologist will all find material of value and interest here. The enormous bibliography alone (one hundred and thirty pages) is ample proof of the wide range of interests the author has covered.

GEORGE K. SMELSER.

Immunity Against Animal Parasites. By James T. Culbertson, M.D. Price, $3.50. Pp. 274, with black and white illustrations and 5 charts and tables. New York: Columbia University Press, 1941.

This book, which presupposes a knowledge of both parasitology and immunology, is designed as a textbook for the student of immunity against animal parasites and as a review and analysis of the recent voluminous literature on the subject for the trained investigator and the practicing physician. While the book is necessarily of limited interest to ophthalmologists it will be of value to those working with tropical diseases of the eye and to laboratory workers concerned with the diagnosis of such occasional parasitic infections of the eye as are seen in the United States.

The book is divided into three parts. Part I is concerned with natural resistance and acquired immunity, part II with immunity to specific diseases and part III with applied immunology. The final

chapter deals with the use of immunologic tests, including the complement fixation reaction, agglutination, precipitation and adhesin and cutaneous tests, in the diagnosis of parasitic infection. Of these the cutaneous tests and the complement fixation reaction appear to be the most valuable.

PHILLIPS THYGESON.

Die entschädigungspflichtigen Berufskrankheiten des Auges. (Supplement to *Klinische Monätsblatter für Augenheilkunde,* vol. 99.) By Prof. Dr. Paul Junius. Price, $1.80. Stuttgart: Ferdinand Enke, 1937.

This is a copy of the laws adopted in Germany on April 1, 1937 on accident insurance for occupational diseases. Every physician in Germany is compelled to report each case of occupational disease that he encounters in his practice. The form in which this report should be made out is given, and the occupational diseases are described which particularly interest the ophthalmologist, such as diseases caused by lead, benzene, roentgen rays and radium, cataract in workers in glass, iron foundries and metal-smelting processes and infectious diseases occurring in persons employed in hospitals, laboratories, etc.

This is an instructive article which deals with a subject that will undoubtedly be taken up more fully in this country.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Consolacao, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. A. J. Ballantyne, 11 Sandyford Pl., Glasgow, C. 3, Scotland.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. Jacques Tupinambo, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cezario Motta St.—112, São Paulo, Brazil.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Lawrence T. Post, 508 N. Grand Blvd., St. Louis, Mo.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Atlantic City. Time: June 8-12, 1942.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank R. Spencer, Physicians' Bldg., Boulder, Colo.
President-Elect: Dr. Ralph I. Lloyd, 14–8th Ave., Brooklyn.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Allen Greenwood, 82 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. D. G. Hugo, 130 Main St., Oshkosh.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Land O'Lakes. Time: June 1942.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Ralph A. Fenton, 1020 S. W. Taylor St., Portland, Ore.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Portland, Ore. Time: May 11-14, 1942.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. H. Elmer, 321 W. State St., Rockford, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. L. Chester McHenry, Medical Arts Bldg., Oklahoma City.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.
Place: Richmond, Va. Time: November 1942.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.
Place: Albuquerque, N. Mex. Time: November 1942.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOY AND OTOLARYNGOLOGY

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. A. L. Hammerel, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Place: Columbia. Time: November 1942.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m. fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. W. J. Abbott, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. L. V. Johnson, 2065 Adelbert Rd., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. A. Nelson, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Harvey E. Dowling, 2414 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. James M. Dunn, 1352 Union St., Schenectady.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John Osburn, 523 W. 6th St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John W. Truitt, 161 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Kaufman Schlivek, 1016–5th Ave., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. James W. Smith, 1016–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. J. Clyde Markel, 200–9th St., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. James E. Landis, 232 N. 6th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.
Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. Roy Seeley Moore, 1704 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N. W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.